UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

MEIJER, INC. and MEIJER DISTRIBUTION, INC., on behalf of themselves and all those similarly situated, *Plaintiff,* v. ALLERGAN, INC., *Defendant.*	Civil Action No.:

COMPLAINT AND JURY DEMAND

TABLE OF CONTENTS

I. INTRODUCTION

1. This action arises from Allergan, Inc.'s ("Allergan") scheme to unlawfully prolong its monopoly over the sale of cyclosporine ophthalmic emulsion, 0.05% in the United States. The lawsuit seeks damages on behalf of the plaintiffs, Meijer Inc. and Meijer Distribution, Inc. ("Meijer"), which are collectively referred to as "Plaintiffs," and a proposed class of purchasers that bought Restasis (Allergan's brand of cyclosporine ophthalmic emulsion, 0.05%) directly from Allergan from May 2014 to the present.

2. Allergan violated sections 1 and 2 of the Sherman Act, 15 U.S.C. §§ 1 & 2, through a scheme to monopolize that involved a series of unlawful acts.

3. *Fraud on the PTO*. Although it had legitimate patent coverage for Restasis through May 2014, Allergan obtained a second wave of patents for Restasis by defrauding the United States Patent and Trademark Office ("PTO"). This fraud unlawfully extended the term of patent coverage for Restasis by many more years. Allergan misrepresented to the PTO that clinical trials of a lower strength Restasis formulation showed unexpected effectiveness and surprising results. But these clinical representations were false. In reality, Allergan derived these representations by cherry-picking unreliable test results while ignoring the vast majority of results that did not support its claims. Allergan also failed to tell the PTO that the outcomes it relied on lacked statistical significance *according to Allergan's own statistical analysis as reported to the FDA*. What's more, Allergan misled the PTO to believe this data was newly discovered, when, in fact, it had been published a decade earlier and was prior art to the second wave Restasis patents. Not knowing the truth about Allergan's "data," the PTO relied on Allergan's misrepresentations and issued the second wave patents.

4. *Wrongful Orange Book listings*. Allergan listed the second wave patents in the Food and Drug Administration's ("FDA") Orange Book despite knowing that those patents did

not fall under the FDA's listing requirements and should not have been asserted against potential generic competitors. Those patents had been procured by fraud, and Allergan knew it. As a result, Allergan knew it was not entitled to the protections the Orange Book affords patent holders. These Orange Book listings were also wrongful because no reasonable company in the position of Allergan could have realistically expected to prevail on the merits of litigation enforcing those patents: the invalidation of the second wave patents was inevitable because Allergan misrepresented the data it relied on and this data was, in fact, prior art.

5. *Wrongful FDA petitions*. Allergan filed baseless petitions with the FDA seeking to have the FDA impose over a dozen unnecessary, time-consuming, and unsupported requirements upon would-be generic competitors. The petitions, along with numerous supplements, diverted substantial resources of the FDA to answering Allergan's demands and delayed the entry of generic competitors. Eventually the FDA, in emphatic language, denied every substantive Allergan demand.

6. *Wrongful patent enforcement*. Using the listed, second wave patents, Allergan filed and pursued at least seven infringement actions against would-be makers of generic Restasis. Allergan knew no reasonable litigant would have a realistic expectation of prevailing on the ultimate merits of those cases. But Allergan's purpose in filing and pursuing the suits was not to achieve ultimate patent victories; it was to frustrate the FDA's review of pending applications for generic cyclosporine ophthalmic emulsion, 0.05% and to delay the ability of generics to enter that market.

7. *Conspiracy to monopolize and contract in restraint of trade*. After the PTO ruled that the second wave patents were likely to be declared invalid during an *inter partes* review, Allergan purported to transfer ownership of the second wave patents to the Saint Regis Mohawk

Tribe ("Mohawk"). The sole purpose of this transfer was to hide under Mohawk's cloak of sovereign immunity and defeat the PTO's jurisdiction over the patents, nullifying the PTO's ability to invalidate them. The Allergan-Mohawk agreement was undertaken to restrain competition unreasonably.

8. Allergan's anticompetitive scheme had its intended consequence: it delayed generic competition in the market for cyclosporine ophthalmic emulsion, 0.05%. But for Allergan's unlawful scheme, generic manufacturers of cyclosporine ophthalmic emulsion, 0.05% would have entered the market as early as May 2014, providing Plaintiffs and other members of the class with access to far less expensive, generic versions of Restasis. Given Restasis's approximate annual sales of $1 billion, the proposed direct purchaser class was likely overcharged by many hundreds of millions of dollars as a result of Allergan's anticompetitive scheme.

II. PARTIES

1. Plaintiffs Meijer, Inc. and Meijer Distribution, Inc., (collectively, "MEIJER") are corporations organized under the laws of the state of Michigan, with their principal place of business located at 2929 Walker Avenue, NW, Grand Rapids, Michigan 49544. Meijer is the assignee of the claims of Frank W. Kerr Co. and McKesson Corporation, which, during the relevant period, purchased Restasis directly from Allergan at supra-competitive prices as a result of Allergan's scheme.

2. The defendant, Allergan, Inc., is a Delaware corporation with its principal place of business located in Irvine, California. Allergan is the holder of approved New Drug Application No. 50-790 for cyclosporine ophthalmic emulsion, 0.05%, sold under the Restasis trademark. Allergan was also the applicant for, and holder of, the six second wave patents which it claims cover Restasis: U.S. Patent No. 8,629,111 (issued January 14, 2014); U.S. Patent No.

8,633,162 (issued January 21, 2014); U.S. Patent No. 8,642,556 (issued February 4, 2014), U.S. Patent No. 8,648,048 (issued February 11, 2014), U.S. Patent No. 8,685,930 (issued April 1, 2014), and U.S. Patent No. 9,248,191 (issued February 2, 2016). As of September 8, 2017, Allergan purports to have transferred its ownership interests in the second wave patents to Mohawk.

3. All of the actions described in this complaint are part of, and in furtherance of, the unlawful conduct alleged herein and were authorized, ordered, or undertaken by Allergan's officers, agents, employees, or other representatives while actively engaged in the management of Allergan's affairs and within the course and scope of their duties and employment or with Allergan's actual, apparent, or ostensible authority.

III. JURISDICTION AND VENUE

4. The Court has subject matter jurisdiction under 28 U.S.C. §§ 1331, 1337(a) and 15 U.S.C. § 15. This action alleges violations of sections 1 and 2 of the Sherman Act, 15 U.S.C. §§ 1 & 2. Those violations are actionable under sections 4 and 16 of the Clayton Act, 15 U.S.C. §§ 15(a) & 26. This complaint seeks an injunction and to recover treble damages, interest, and costs of suit and attorneys' fees due to Allergan's unlawful foreclosure of generic competition in the market for cyclosporine ophthalmic emulsion, 0.05% in the United States.

5. Venue is proper in this District pursuant to 28 U.S.C. § 1391(b), (c), and (d). During the class period (May 2014 to the present), Allergan resided, transacted business, was found, or had agents in this District. A substantial portion of the wrongdoing alleged in this complaint affected interstate trade and commerce, and was carried out in this District. Allergan maintained and continues to maintain significant offices and operations within 30 miles of this Court's Brooklyn courthouse, including its "US Administrative Headquarters" in Madison, New Jersey and its US sales operations offices in Jersey City, New Jersey.

6. This Court has personal jurisdiction over Allergan. Allergan's wrongful conduct had a substantial effect on interstate commerce of the United States, including in this District. During the class period, Allergan manufactured, sold, and shipped Restasis in a continuous and uninterrupted flow of interstate commerce, which included sales of Restasis in and from this District, advertisement of Restasis in media in this District, monitoring prescriptions of Restasis by prescribers within this District, and employment of product detailers in this District, who as agents of Allergan marketed Restasis to prescribers in this District. Allergan's conduct had a direct, substantial, and reasonably foreseeable effect on interstate commerce, including commerce within this District.

7. Throughout the United States and including in this District, Allergan transacted business, maintained substantial contacts, or committed overt acts in furtherance of the illegal scheme. The scheme has been directed at, and has had the intended effect of, causing injury to persons residing in, located in, or doing business throughout the United States, including in this District.

IV. REGULATORY BACKGROUND

A. New Drug Applications and Orange Book Listings

8. Under the Food, Drug, and Cosmetics Act ("FDCA"), drug companies who wish to sell a new drug product must file a New Drug Application ("NDA") with the FDA. An NDA submission must include specific data concerning the safety and effectiveness of the drug.

9. Under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Amendments"),[1] an NDA applicant must submit to the FDA information on

[1] Pub. Law No. 98-417, 98 Stat. 1585 (1984).

each patent that covers the drug or methods-of-use described in the NDA and for which "a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug."[2] The FDA then publishes this information in a digest titled *Approved Drug Products with Therapeutic Equivalence Ratings* but known as the Orange Book. The statute further provides that if a drug patent is issued after NDA approval, the NDA sponsor must file that new patent information with FDA no later than 30 days after the date the patent is issued.[3]

10. The FDA performs only a ministerial act in listing the patents a brand manufacturer identifies in the Orange Book. The FDA does not have the resources or authority to verify the manufacturer's representations for accuracy or trustworthiness. Thus, the FDA relies completely on the manufacturer's truthfulness about the Orange Book information it supplies, including whether the listed patent is valid and may reasonably be asserted against a generic applicant.

11. Once a brand manufacturer lists a patent in the Orange Book, that listing puts potential generic competitors on notice that the brand considers the patent to cover its drug. And the listing triggers important regulatory consequences.

B. Abbreviated New Drug Applications and the Hatch-Waxman Amendments

12. Congress passed the Hatch-Waxman Amendments to balance the need to provide brand companies with incentives to develop new medicines against the countervailing need to speed the entry of cheaper, equally effective versions of these medications.

13. Designed to ensure the timely introduction of generic drugs onto market, the

[2] 21 U.S.C. § 355(b)(1), (c)(2).

[3] *Id.* § 355(c)(2).

Hatch-Waxman Amendments enable generic manufacturers to file Abbreviated New Drug Applications ("ANDA") with the FDA for drugs they seek to bring to market. Rather than requiring generic manufacturers to conduct expensive clinical trials to re-prove the drugs' safety and efficacy, the Hatch-Waxman Amendments allow generic manufacturers to rely on the data the brands have already submitted to prove the drugs' safety and efficacy. All a generic manufacturer must show is that its generic copies are pharmaceutically-equivalent and bioequivalent (together, "therapeutically equivalent") to the brand. The premise – codified by Congress and implemented by the FDA for the past thirty years – is that two drug products that contain the same active pharmaceutical ingredient, in the same dose, and delivered in the same way are equally safe and effective.

14. The Hatch-Waxman Amendments also provided a vehicle through which a generic manufacturer can address the drug product and method-of-use patents that cover the drug it seeks to manufacture. An ANDA applicant must include in its application one of the following four certifications with respect to the patents covering the branded drug it seeks to produce:

i. That such patent information has not been filed (a "Paragraph I certification");

ii. That such patent has expired (a "Paragraph II certification");

iii. The date on which such patent will expire (a "Paragraph III certification"); or

iv. That such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted (a "Paragraph IV certification").[4]

15. After an ANDA applicant submits its application along with its certification, the FDA decides whether to accept the application. Once an application containing a Paragraph IV

[4] *Id.* § 355(j)(2)(A)(vii)(I)-(IV); *see also* 21 C.F.R. 314.94(a)(12)(i)(A). The FDCA provides only one circumstance in which an applicant with a pending ANDA need not certify to a listed patent, but that exception, relating to method-of-use patents, is not applicable here. 21 U.S.C. § 355(j)(2)(A)(viii).

certification receives acknowledgment from the FDA that the agency has determined the application is sufficiently complete to permit substantive review, the applicant must provide the NDA holder and the patent owner notice of its Paragraph IV certification. This notice must include a description of the legal and factual basis for the ANDA holder's assertion that the patent is invalid or not infringed.[5] The statute prohibits an applicant from providing such notice prior to FDA's formal receipt of the application for substantive review.[6]

16. If an NDA holder or patent owner initiates a patent infringement action against an ANDA applicant within 45 days of receiving that applicant's Paragraph IV notice, approval of the applicant's ANDA will generally be stayed for 30 months from the date of the notice or such shorter or longer time as the court might order.[7] If a patent is listed in the Orange Book after an ANDA is submitted but before it is approved, the applicant for the pending ANDA generally must amend its application and provide an appropriate certification for the newly listed patent and the attendant notice. Nonetheless, a patent listed after the date an ANDA was accepted for filing (i.e., the date the FDA determines it was substantially complete) will not trigger a 30-month stay for that application.[8]

---

[5] *Id.* § 355(j)(2)(B)(iv)(II).

[6] *Id.* § 355(j)(2)(B)(ii).

[7] *Id.* § 355(j)(5)(B)(iii). The brand manufacturer could file patent infringement claims more than 45 days after receiving the Paragraph IV certification, but doing so would not trigger the automatic 30-month stay of FDA approval.

By enabling a brand manufacturer to bring suit in response to a Paragraph IV certification, the Hatch-Waxman Amendments create a procedural mechanism through which the brand and generic manufacturer can resolve their patent dispute *before* the generic's intended launch date. Thus, such a system prevents the delay to generic entry that such a suit would otherwise cause.

[8] *Id.* § 355(j)(5)(B)(iii). The applicable text reads that, if there is a Paragraph IV certification:

> [T]he approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice . . . is

17. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003[9] revised these exclusivity provisions. These revisions, like the original Hatch-Waxman Amendments, provide the "first applicant" to submit a substantially complete application that contains a Paragraph IV certification – the first applicant to undertake the risk of patent infringement litigation – an incentive to undertake that risk in the form of the opportunity to be the *only* generic drug manufacturer on the market with the brand for a 180-day period. Under these provisions, the first generic manufacturer to file a Paragraph IV-certified ANDA gains 180 days of exclusivity. Subsequent ANDA applicants for the same product that contain Paragraph IV certifications cannot be approved until after this six-month exclusivity has run (unless the first applicant has forfeited this period).[10]

18. The FDCA defines "first applicant" as "an applicant that, on the first day on which a substantially complete application containing a [Paragraph IV] certification . . . is submitted for approval of a drug, submits a substantially complete application that contains and

> received, an action is brought for infringement of the patent . . . before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice . . . or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action . . . .

Id. The statute provides exceptions to the 30-month stay, including various litigation or settlement scenarios that occur before the 30-month period expires. *Id.*

[9] Pub. L. No. 108-173, 117 Stat. 2066 (Dec. 8, 2003).

[10] The requirements for obtaining and retaining this 180-day exclusivity period are described at 21 U.S.C. § 355(j)(5)(B)(iv), (j)(5)(D).

lawfully maintains a [Paragraph IV] certification . . . for the drug."[11]

19. There are six different ways a first applicant can forfeit his or her 180-day period of exclusivity. The last, regarding patent expiration, provides that a forfeiture event occurs if "[a]ll of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired."[12] Notably, "[i]f all first applicants forfeit the 180-day exclusivity period under [21 U.S.C. § 355(j)(5)(D)(ii)] . . . no applicant shall be eligible for a 180-day exclusivity period."[13]

C. The FDA's Determination of Bioequivalence for ANDAs

20. *ANDA approvals.* The Hatch-Waxman Amendments created Section 505(j)[14] of the FDCA: the ANDA approval pathway for generic drugs. To obtain approval, an ANDA applicant is not required to provide independent evidence of the safety and efficacy of its proposed generic drug product. Instead, the applicant relies on the FDA's previous finding that the brand drug (known in this setting as the "reference listed drug") is safe and effective. An ANDA applicant must show its generic product is bioequivalent to the reference listed drug, i.e., that the drug product described in the ANDA contains the same active ingredient, conditions of use, route of administration, dosage form, strength, and (with certain permissible differences) labeling as the reference listed drug.[15]

21. *Regulations provide exacting requirements for ophthalmic ANDAs*. The FDA will

[11] *Id.* § 355(j)(5)(B)(iv)(II)(bb).

[12] *Id.* § 355(j)(5)(D)(i)(VI).

[13] *Id.* § 355(j)(5)(D)(iii).

[14] *Id.* § 355(j).

[15] *Id.* § 355(j)(2)(A)(iv); *see also* 21 C.F.R. 314.94(a)(7).

refuse to approve an ANDA if it determines that "the inactive ingredients of the drug are unsafe for use" as labeled, or if "the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included."[16] The FDA considers the inactive ingredients or composition of a proposed generic drug product unsafe "if, on the basis of information available to the agency, there is a reasonable basis to conclude that one or more of the inactive ingredients of the proposed drug or its composition raises serious questions of safety or efficacy."[17]

22. In general, the inactive ingredients in a generic topical product need not match those in the reference listed drug so long as the applicant "identifies and characterizes [any] differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product."[18] However, generic versions of drugs intended for ophthalmic use, like Restasis, face stricter requirements. Specifically, generic ophthalmic drug products must "contain the same inactive ingredients and in the same concentration as the reference listed drug."[19] However, the applicant's product can differ from the reference listed drug in its "preservative, buffer, substance to adjust tonicity, or thickening agent provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product."[20] The FDA considers an inactive ingredient in a proposed generic version of an ophthalmic drug "unsafe"

[16] 21 U.S.C. § 355(j)(4)(H); *see also* 21 C.F.R. 314.127(a)(8)(ii)(A).

[17] 21 C.F.R. § 314.127(a)(8)(ii)(A).

[18] *Id.* § 314.94(a)(9)(v).

[19] *Id.* § 314.94(a)(9)(iv).

[20] *Id.*

unless it is the same concentration (other than allowable differences) as the reference listed drug. The FDA also considers the generic unsafe if the applicant fails to demonstrate that any allowable difference does not affect the safety or efficacy of the proposed product.[21]

23. The FDA will not approve an ANDA if an inactive ingredient or the composition of the proposed drug is unsafe under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug.[22]

24. *Determining bioequivalence*. An ANDA applicant must also demonstrate that its proposed generic drug is bioequivalent to the reference listed drug.[23] The FDCA states that a generic drug is bioequivalent to the listed drug if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses."[24]

25. But "for a drug that is not intended to be absorbed into the bloodstream, the Secretary may establish alternative, scientifically valid methods to show bioequivalence if the alternative methods are expected to detect a significant difference between the drug and the listed drug in safety and therapeutic effect."[25] Thus, a showing that the active ingredient or therapeutic

---

[21] *Id.* § 314.127(a)(8)(ii)(C).

[22] 21 U.S.C. 355(j)(4)(H); 21 C.F.R. §§ 314.94(a)(9)(ii), 314.127(a)(8)(i).

[23] *See, e.g.*, 21 U.S.C. § 355(j)(2)(A)(iv) (requiring "information to show that the new drug is bioequivalent to the listed drug"); 21 C.F.R. 314.94(a)(7) (requiring, as part of ANDA content and format, information to show that the drug product is bioequivalent to the reference listed drug); 21 C.F.R. 314.127(a)(6)(i) (providing that FDA will refuse to approve an ANDA if information submitted is insufficient to show that the drug product is bioequivalent to the reference listed drug referred to in the ANDA).

[24] 21 U.S.C. § 355(j)(8)(B)(i); *see also* 21 C.F.R. § 320.23(b).

[25] 21 U.S.C. § 355(j)(8)(C).

ingredient in the proposed generic drug reaches the site of drug action at a rate and to an extent not significantly different from that of the reference listed drug, along with other information required for approval, permits the FDA to conclude that the proposed generic drug can be expected to perform the same way in the body as the reference listed drug.

26. Bioequivalence testing determines whether differences in formulation (e.g., differences in inactive ingredients) between a proposed generic drug and the reference listed drug have an impact on the rate and extent to which the active ingredient becomes available at the site of action. The statute, regulations, and case law give the FDA considerable flexibility in determining how the bioequivalence requirement is met. The testing methods may include in vivo data (data from a study on live subjects), in vitro data (data from laboratory studies), or both.[26] The selection of the method used to meet an in vivo or in vitro testing requirement depends upon the purpose of the study, the analytical methods available, and the nature of the drug product. Applicants are required to conduct bioavailability and bioequivalence testing using the most accurate, sensitive, and reproducible approach available. The method used must be capable of measuring bioavailability or establishing bioequivalence, as appropriate, for the product being tested.[27]

---

[26] *See id.* § 355(j)(7)(A)(i)(III); *see also Schering Corp. v. Food & Drug Admin.*, 51 F.3d 390, 398 (3d Cir. 1995) (noting that this provision "vests the FDA with discretion to determine whether *in vitro* or *in vivo* bioequivalence studies, or both, will be required for the approval of generic drugs under the abbreviated application processes").

[27] 21 C.F.R. § 320.24(a). In the preamble to the 1992 final rule, FDA explained that, depending upon the drug, it would determine the appropriate bioequivalence methodology on a case-by-case basis: "Bioequivalence can be established by pharmacodynamic measurement as well as by in vitro techniques and bioequivalence studies with clinical endpoints. The preferred method for establishment of bioequivalence . . . is determined on a case-by-case basis, depending on the drug under study." Abbreviated New Drug Application Regulations, 57 Fed. Reg. 17950, 17972 (Apr. 28, 1992) (codified at 21 C.F.R. § 320.24).

27. Section 320.24(b) of FDA's regulations describes preferred bioequivalence methods in descending order of "accuracy, sensitivity, and reproducibility."[28] They include: (1) in vivo pharmacokinetic studies in "whole blood, plasma, serum, or other appropriate biological fluid," or in vitro tests that have been correlated with and are predictive of human in vivo bioavailability data;[29] (2) in vivo studies in which "urinary excretion of the active moiety, and, when appropriate, its active metabolite(s), are measured";[30] (3) in vivo pharmacodynamic effect studies;[31] (4) clinical endpoint studies;[32] and (5) in vitro studies acceptable to the FDA that ensure human in vivo bioavailability.[33]

28. In addition, and consistent with § 505(j)(8)(C) of the FDCA,[34] 21 C.F.R. § 320.24(b)(6) states that the FDA has the authority to use "[a]ny other approach deemed adequate by FDA to . . . establish bioequivalence."[35] For some drug products, adequate methods for demonstrating bioequivalence have not yet been developed. In such cases, the FDA will not approve an ANDA.

29. The FDA's authority to make bioequivalence determinations on a case-by-case basis using in vivo, in vitro, or both types of data enables it to effectuate several long recognized

---

[28] 21 C.F.R. § 320.24(b).

[29] *Id.* § 320.24(b)(1)(i)-(ii).

[30] *Id.* § 320.24(b)(2).

[31] *Id.* § 320.24(b)(3).

[32] *Id.* § 320.24(b)(4).

[33] *Id.* § 320.24(b)(5).

[34] 21 U.S.C. § 355(j)(8)(C).

[35] 21 C.F.R. § 320.24(b)(6); *see also Astellas Pharma US, Inc. v. Food & Drug Admin.*, 642 F. Supp. 2d 10, 20 (D.D.C. 2009) (quoting 21 C.F.R. § 320.24(b) in upholding the FDA's sameness determination of a generic drug product).

policies that protect the public health: (1) refraining from unnecessary human research when other methods of demonstrating bioequivalence meet the statutory and regulatory standards for approval;[36] (2) permitting it to use the latest scientific advances in approving drug products;[37] (3) protecting the public by ensuring only safe effective generic drugs are approved for marketing;[38] and (4) making more safe and effective generic drugs available.[39]

30. *Principles of bioequivalence for locally acting products*. For systemically acting drug products, the rate and extent of systemic absorption of the drug is usually the most sensitive, accurate, and reliable indicator of the rate and extent to which the active ingredient becomes available at the site of drug action. The determination of the bioequivalence of a drug product whose primary mechanism of action depends on systemic absorption generally rests on a comparison of the drug and/or metabolite concentrations in an accessible biological fluid, such as blood or urine, after administration of a single dose or multiple doses of the drug product to

[36] 21 C.F.R. § 320.25(a) (stating that a "guiding principle" for the conduct of an in vivo bioavailability study is that "that no unnecessary human research should be done"); Abbreviated New Drug Application Regulations, 54 Fed. Reg. 28872, 28883 (July 10, 1989) (in discussing § 320.22, the FDA clarified that it "does not believe Congress intended that unnecessary human research be conducted . . . if the agency concludes that bioequivalence can be demonstrated by in vitro tests, the agency proposes to require only such tests rather than in vivo studies").

[37] Bioavailability and Bioequivalence Requirements: Procedures for Establishing a Bioequivalence Requirement, 42 Fed. Reg. 1624, 1629 (Jan. 7, 1977) ("As with all new regulations relating to an evolving science, the Commissioner reserves the right to consider other factors that may indicate the need to establish a bioequivalence requirement.").

[38] *Schering Corp. v. Sullivan*, 782 F. Supp. 645, 650 (D.D.C. 1992), *opinion vacated on other grounds sub. nom. Schering Corp. v. Shalala*, 995 F.2d 1103 (D.D.C. 1993) (explaining that "ensur[ing] the safety of these drugs before they are substituted for their name-brand counterparts" as one underlying policy goals of the Hatch-Waxman Amendments).

[39] *Fisons Corp. v. Shalala*, 860 F. Supp. 859, 866-67 (D.D.C. 1994) (explaining that the bioequivalence waiver provision "comports with the structure and broader policy objectives of the Hatch-Waxman Act," including making safe and affordable generic drugs available); *Schering*, 782 F. Supp. at 650 (noting that the purposes of Hatch-Waxman Amendments are "to make more inexpensive generic drugs available" and "to ensure the safety of these drugs").

healthy volunteers.[40]

31. By contrast, a traditional in vivo bioequivalence study comparing the rate and extent of absorption of the active ingredient into the blood stream is usually of limited utility for locally acting, non-systemically absorbed drug products. In certain instances, therefore, the FDA has determined that an ANDA applicant for such a product may establish bioequivalence using in vivo studies with a clinical endpoint or endpoints. In addition, for certain locally acting, non-systemically absorbed products with formulations having the same qualitative and quantitative composition as the reference listed drug, the FDA has determined that an ANDA applicant may demonstrate bioequivalence using specified in vitro methods.

32. The choice of appropriate bioequivalence study design is based on the ability of the study to compare the drug delivered by the two products at the particular site of action of the drug.

33. Congress intended to grant the FDA wide discretion to establish bioequivalence standards on a drug-by-drug basis when it enacted the Hatch-Waxman Amendments. And the courts have recognized the FDA's discretion to determine how the bioequivalence requirement should be met for a product or class of products, so long as the FDA's determination is not contrary to the governing statute and regulations and is based on a "reasonable and scientifically supported criterion."[41] Courts that have considered the FDA's bioequivalence determinations

[40] 21 U.S.C. § 355(j)(8); Food & Drug Admin., Guidance for Industry: Bioavailability and Bioequivalence Studies for Orally Administered Drug Products – General Considerations 6 (Mar. 2003), *available at* https://www.fda.gov/ohrms/dockets/ac/03/briefing/3995B1_07_GFI-BioAvail-BioEquiv.pdf.

[41] *Schering*, 782 F. Supp. at 651; *see also Fisons*, 860 F. Supp. at 866-67 ("[T]he factual determination of how bioequivalence is determined properly rests within the FDA's discretion.").

have consistently upheld the aspects of the FDA's implementation of the FDCA's bioequivalence requirements at issue in those cases.[42]

34. *Bioequivalence guidance*. In June of 2010, the FDA issued a guidance for the industry entitled "Bioequivalence Recommendations for Specific Products."[43] This guidance described the FDA's process of providing guidance to applicants on the design of bioequivalence studies for specific drug products. Prior to establishing the product-specific bioequivalence guidance mechanism outlined in the Bioequivalence Specific Product Guidance, the FDA only provided recommendations on the design of bioequivalence studies for specific products to parties who expressly requested such information.

35. The FDA periodically publishes notices in the Federal Register announcing the availability of draft, revised draft, and final versions of product-specific bioequivalence recommendations. These notices identify a comment period for draft bioequivalence recommendations.[44]

36. The FDA considers comments received on product-specific bioequivalence recommendations in developing its final recommendations. As with FDA guidance in general, these recommendations describe the FDA's "current thinking" and should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. Applicants following product-specific bioequivalence recommendations have an expectation that the FDA

[42] *See, e.g.*, *Schering*, 782 F. Supp. at 650-51; *Fisons*, 860 F. Supp. at 866-87.

[43] Food & Drug Admin., Guidance for Industry: Bioequivalence Recommendations for Specific Products (June 2010), http://www.fda.gov/downloads/ucm072872.pdf.

[44] 21 C.F.R. § 10.115(d)(3) ("Although [final] guidance documents do not legally bind FDA, they represent the Agency's current thinking. Therefore, FDA employees may depart from guidance documents only with appropriate justification and supervisory concurrence.").

will agree that their approach to establishing bioequivalence is appropriate.[45] However, applicants may confer with the agency on use of different approaches for establishing bioequivalence.

37. Recommendations made in a draft or final guidance does not bind the FDA or the public. Further, even in the absence of product-specific bioequivalence guidance, the FDA has the authority to approve a product supported by bioequivalence data that meets the statutory and regulatory requirements.

D. The Economics of Bioequivalent, Generic Drugs

38. Because generic versions of brand-name drugs contain the same active ingredients, and are determined by the FDA to be just as safe and effective as their branded counterparts, the only material differences between generic drugs and their branded counterparts are their prices and manufacturers. Because generic versions of branded products are commodities that cannot be differentiated, the primary basis for generic competition is price.

39. Typically, generics are at least 25% less expensive than their branded counterparts when there is a single generic competitor. They are 50% to 80% (or more) less expensive when there are multiple generic competitors on the market for a given brand. Consequently, the launch of a bioequivalent generic drug usually results in significant cost savings to all drug purchasers.

40. Since the passage of the Hatch-Waxman Amendments, every state has adopted substitution laws that either require or permit pharmacies to substitute generic equivalents for branded prescriptions (unless the prescribing physician has specifically ordered otherwise).

41. The combination of these factors – the regulatory interchangeability of bioequivalent generics for the brand, state substitution laws, margin incentives of pharmacies,

[45] *Id.*

and the like – results in the typical phenomenon that once a brand drug "goes generic," the product swiftly moves from a monopoly priced to a commodity priced item.

42. Generic competition enables all members of the proposed class to purchase generic versions of the drug at substantially lower prices, and to purchase the brand drug at a reduced price.

43. Until a generic version of the brand drug enters the market, however, there is no bioequivalent generic drug to substitute for and compete with the brand drug, and therefore the brand manufacturer can continue to charge supra-competitive prices. Brand manufacturers, such as Allergan, are well aware of generics' rapid erosion of their brand sales. Brand manufacturers thus seek to extend their monopolies through any means possible, sometimes even resorting to illegal ones.

E. Citizen Petitions to the FDA

44. Section 505(j) of the FDCA creates a mechanism through which a person may file a petition with the FDA requesting the agency take, or refrain from taking, any form of administrative action. This mechanism is commonly referred to as a "citizen petition." These petitions, when used as intended, provide an opportunity for individuals to express their genuine concerns about safety, scientific, or legal issues regarding a product before, or after, its market entry.

45. The filing of a citizen petition with the FDA imposes a burden on the agency. FDA regulations concerning citizen petitions require the FDA to respond to each citizen petition within 180 days of receipt. Those responses may be to approve or deny the requests, in whole or in part. The agency also may provide a tentative response with an estimate on a time for a full response.

46. Reviewing and responding to citizen petitions is a resource-intensive and time-

consuming task. The FDA must research the petition's subject and examine scientific, medical, legal, and sometimes economic issues. The FDA must also coordinate internal agency review and clearance of the petition response. These activities strain the FDA's limited resources.

47. The FDA's longtime practice – well known in the pharmaceutical industry – is to withhold ANDA approval until after the agency has prepared and authorized a response to a citizen petition that bears on the subject of the pending ANDA. And its practice is often to do so regardless of the merit, or lack thereof, of the petition.

48. All too often, brand companies seeking to delay the FDA's review and approval of pending ANDAs through abuse of the citizen petition process. Petitions by rival companies rarely raise legitimate concerns about the safety or efficacy of generic products, and, instead, only seek to preserve monopolies after the end of a statutorily granted patent or FDA exclusivity period.

49. Not only the ultimate futility, but also the timing, of these tactical filings is important: companies frequently file these citizen petitions on the eve of FDA approval of an ANDA for competing generic drugs, even though the petitioner could have made the same arguments months, or even years, before.

50. The filing of petitions by brand companies challenging the FDA's bioequivalence standards or methods also signals the likelihood that the brand will file litigation against the FDA in the event that the FDA approves an ANDA that does not adopt the draconian terms demanded in its petition.

51. As a result, the filing of petitions by brand companies attacking FDA ANDA decision-making disrupts the FDA's ordinary course review of pending ANDAs. This can result in delay of approval of a pending ANDA for considerable periods of time while the FDA

evaluates the merits (or lack thereof) of the petition, prepares a response, and ensures that its positions are adequately prepared for the thinly-veiled threat of litigation.

52. The resulting delay of generic competition can be lucrative for an incumbent brand manufacturer facing impending competition from generics. The cost of filing a baseless citizen petition pales in comparison to the value of securing an additional period of monopoly profits.

53. Abusive and anticompetitive citizen petitions have become an increasingly common problem in the last 15 years, as brand-name companies have sought to compensate for dwindling new product pipelines.

54. The FDA has long acknowledged citizen petition abuse, stating as far back as 2005 that it had "seen several examples of citizen petitions that appear designed not to raise timely concerns with respect to the legality or scientific soundness of approving a drug application, but rather to delay approval by compelling the agency to take the time to consider arguments raised in the petition, regardless of their merits, and regardless of whether the petitioner could have made those very arguments months and months before."[46]

55. Similarly, a former director of the Office of Generic Drugs noted that of 42 petitions raising issues about the approvability of generic products, "very few . . . have presented data or analysis that significantly altered FDA's policies. Of the 42 citizen petition responses examined, *only three petitions* led to a change in [FDA] policy on the basis of data or information submitted in the petition."[47] He further stated that "[i]t is very rare that petitions

[46] 153 Cong. Rec. 127 (Jan. 4, 2007) (statement of FDA Chief Counsel Sheldon Bradshaw in 2005).

[47] Gary Buehler, Dir. of the Office of Generic Drugs, Center for Drug Evaluation and Research, Food and Drug Admin., Statement the before the Senate Special Committee on Aging

present new issues that CDER has not fully considered, but the [FDA] must nevertheless assure itself of that fact by reviewing the citizen petitions."[48]

56. The abuse of the citizen petition process led Congress to add § 505(q) to the FDCA in 2007 through the FDA Amendments Act (the "FDAAA").[49] This section provides that the FDA "shall not delay approval of a pending [ANDA]" because of a citizen petition unless the FDA determines that a delay is "necessary to protect the public health."[50] The FDAAA does not, however, provide the FDA with additional resources that might allow it to more promptly respond to citizen petitions – meaning that a brand-name drug maker can still use the citizen petition process to delay generic approval while the FDA considers whether the company's citizen petition implicates issues of public health, regardless of whether the petition has any real merit.

57. Years after the enactment of the FDAAA, the FDA continues to have serious concerns about the abuse of the citizen petition process for anticompetitive purposes. In a 2012 report to Congress, the FDA stated that it was "concerned that section 505(q) may not be discouraging the submissions of petitions that do not raise valid scientific issues and are intended primarily to delay the approval of competitive drug products."[51] Indeed, recent studies have

---

8 (July 20, 2006) (emphasis added), *available at* https://www.aging.senate.gov/imo/media/doc/hr161gb.pdf.

[48] *Id.*

[49] 21 U.S.C. § 355(q).

[50] *Id.*

[51] Food & Drug Admin., Fourth Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action for Fiscal Year 2011 6 (Dec. 14, 2012), *available at* http://www.hpm.com/pdf/blog/FDA%20FY2011%C20505q%C20CP%20Report.pdf.

found that many petitions from brand drug manufacturers "appear to be last-ditch efforts to hold off generic competition,"[52] and that between 2011 and 2015, the FDA denied 92% of § 505(q) citizen petitions (the type Allergan use here to delay generic entry).[53]

F. Patent Protection and its Limits

58. Brand drug companies develop their drug patent portfolios to maximize their terms of patent protection.

59. There is a predictable pattern to the way brand drug companies develop their patent portfolios. The first group of patents in a brand drug company's portfolio for a particular drug may reflect a genuine technological breakthrough that may later contribute to the success of the drug. These initial patents usually cover the active compound in a prescription drug or a particular pharmaceutical composition.

60. After filing their applications for the initial patents, brand companies continue to seek other forms of patent protection; often filing for narrow modifications relating to specific formulations, methods of using the drugs, or processes for creating the drug products disclosed in the original patent filings. However, for these secondary patent filings, the original patents may become "prior art," limiting the scope of follow-on patents that the brands may obtain. A brand may only obtain a *new* patent on a previously patented drug product if the specific feature the brand seeks is novel and is non-obvious in light of the prior art (older patents, publications, and inventions). As the number of patent filings for the drug grows, so does the volume of prior art that a brand application must distinguish.

---

[52] Robin Feldman, et al., *Empirical Evidence of Drug Pricing Games – A Citizen's Pathway Gone Astray*, 20 Stan. Tech. L. Rev. 39, 70 (2017).

[53] Michael A. Carrier & Carl Minniti, *Citizen Petitions: Long, Late-Filed, and At-Last Denied*, 66 Am. U. L. Rev. 305, 338, 339 tbl. 8 (2016).

61. Therefore, a typical patent portfolio for a brand drug has its most significant patents issuing first. Over time, the later issued patents become increasingly narrow and more difficult to obtain. Even if narrower coverage is obtained, these later issuing patents are more vulnerable to invalidation for covering subject matter that is old or obvious. The narrower coverage is also more easily designed around by generic competitors, thus preventing the brand from satisfying its burden of proving infringement to keep generics out of the market.

62. Because patent prosecutions before the PTO are non-adversarial, patent applicants are subject to special oaths and duties designed to protect the public's interest in the PTO's issuance of valid patents. Because patents usually enable a brand manufacturer to exclude competition and charge supra-competitive prices during the patent term, it is crucial that any patent underlying a branded drug be valid and lawfully obtained.

63. To help ensure the "public interest is best served," patent applicants are subject to the duty of disclosure, candor, and good faith, which requires the applicant to disclose to the PTO "all information known to be material to patentability," including any prior art.[54] This duty is imposed on those responsible for making the application, including each of the named inventors; each "attorney or agent who prepares or prosecutes the application"; and "[e]very other person who is substantively involved in the preparation or prosecution of the application."[55] Failure to adhere to these duties of candor and good faith can result in a court finding that a patent is invalid and unenforceable for inequitable conduct, and subject the patent owner to other penalties, such as fee shifting of attorneys' fees.[56]

[54] *See* 37 C.F.R. § 1.56(a).

[55] *Id.* § 1.56(c).

[56] 35 U.S.C. § 285.

G. The *Inter Partes* Review System

64. In 2011, Congress passed the Leahy-Smith America Invents Act ("AIA") to address a widely held concern that invalid patents were being issued and enforced, to the detriment of both innovation and the economy.

65. A centerpiece of the AIA is the system of *inter partes* review. Through this system at the PTO, members of the public can, challenge improperly issued patents. The advent of *inter partes* review vastly expands the universe of patent challengers, ensuring that many patents that should not have been granted are challenged and invalidated. This system also creates a less expensive and more efficient venue for patent validity challenges than challenges in district court. *Inter partes* review proceedings are overseen by technically educated judges, skilled in the sciences of a particular proceeding.

66. An *inter partes* review commences when a party – often an alleged patent infringer – petitions the Patent Trial and Appeals Board ("Board") to reconsider the PTO's issuance of an existing patent and invalidate it on the ground that it was obvious or anticipated by prior art.

67. The Board will grant such a request for an *inter partes* review only if the challenger of the patent shows "a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition."[57] The Board must decide the review within one year of the institution date.

68. The Board proceedings have become an exceedingly effective method of challenging improperly granted patents: *only 4%* of all Board petitions end with a final written

[57] 35 U.S.C. § 314(a).

decision in which all claims are upheld as patentable[58]; 69% of all Board petitions that have reached final written decisions have led to findings that *all* of the patents' claims were unpatentable.[59]

H. General Principles

69. From this framework, some basic rules emerge.

70. First, brand drug companies may pursue only valid patents and must act with candor and forthrightness in their dealings with the PTO.

71. Second, brand drug companies may not provide false or misleading information to the FDA and then use that information to delay entry of less expensive generic medications.

72. Third, drug companies may not file patent infringement lawsuits against would-be competitors when the action has no realistic likelihood of success on the merits; the mere filing of such a lawsuit delays legitimate efforts to gain market entry.

73. Finally, patent holders may not knowingly use invalid patents as anticompetitive weapons and evade the consequences; federal policy favors prompt invalidation of improvidently issued patents.

74. Allergan broke all of these basic rules.

V. FACTS

75. Plaintiffs allege the facts in the complaint on the basis (a) of personal knowledge as to those facts relating to it, (b) of investigation by counsel based on publicly available facts drawn from FDA and PTO records, litigation files, SEC filings and statements, and other

[58] Steve Brachmann & Gene Quinn, *Are More than 90 Percent of Patents Challenged at the PTAB Defective?*, IP Watch Dog (June 14, 2017), http://www.ipwatchdog.com/2017/06/14/90-percent-patents-challenged-ptab-defective/id=84343/.

[59] *Id.*

publicly available records, and (c) the proceedings and decisions of the district court in the Eastern District of Texas, including the ruling on the patent invalidity of the second wave patents in *Allergan, Inc. v. Teva Pharmaceuticals USA, Inc.* ("*Allergan*").[60]

76. Allergan manufactures and sells an important dry-eye medication called Restasis. Since its launch in 2003, Allergan's Restasis has become one of the most important dry eye treatments. In fact, it is one of the most commonly prescribed drugs in the world: last year, Restasis reached nearly $1.5 billion in U.S. sales alone.

77. Restasis is an emulsion treatment (a mixture of two or more liquids that are normally unblendable) consisting of: 0.05% by weight cyclosporin A[61] (an immunosuppressant), 1.25% by weight castor oil, 0.05% by weight pemulen (an emulsion stabilizer), 1% by weight polysorbate 80 (an emulsifier), and 2.2% by weight glycerin. Allergan branded this emulsion as Restasis, with cyclosporin A acting as the active ingredient.

78. Dry eye is a group of conditions that occur when the human eye fails to produce enough (qualitatively or quantitatively) tears components or when other factors interfere with the maintenance of an adequate tear film. These conditions cause patients discomfort, blurred vision, and infection. If left untreated, dry eye can sometimes lead to serious complications that threaten vision.

79. There are many different etiologies of dry eye. One common form is aqueous-deficient dry eye, known as keratoconjunctivitis sicca (KCS), which is often associated with

[60] No. 2:15-cv-01455-WCB, 2017 WL 4803941 (E.D. Tex. Oct. 16, 2017).

[61] Cyclosporin A is sometimes spelled "cyclosporine" to distinguish it from other cyclosporins, such as cyclosporins B, C, and D. *Id.* at *3 n.3.The generic name for Restasis is cyclosporine ophthalmic emulsion, 0.05%. This complaint refers to cyclosporin A as "cyclosporine" or "cyclosporin A."

inflammation. An even more common cause of dry eye is evaporative dry eye, where the quantity of aqueous tears a person produces is adequate, but a deficiency in the quantity or quality of the eye's lipid layer leads to rapid evaporation. Other causes of dry eye include: eyelid malposition, traumatic injury to the eyelids or lacrimal system, decreased aqueous tear secretion due to side effects of systemic drugs, and congenital autonomic nervous system disorders leading to decreased tear secretion. Although the different etiologies of dry eye conditions may sometimes exhibit similar clinical findings, including inflammation, many conditions are not inflammatory, at least in their initial stages.

80. Ophthalmologists use a number of different tests and indicators to diagnose and measure dry eye conditions. One commonly used diagnostic device is the Schirmer tear test, which entails placing a strip of filter paper under a patient's eyelid and measuring how many millimeters of the paper are wetted by the patient's tears within five minutes. The Schirmer tear test can be conducted with or without an ocular anesthetic. But conducting the test with anesthesia is considered a better test of the patient's basal tearing (i.e., the tear production that occurs continuously and naturally in the absence of any unusual stimulation). Conducting a Schirmer test without anesthesia provides a measure of basal tearing plus "reflex tearing" (i.e., tearing that results in response to an irritant in the eye, such as a piece of filter paper under the eyelid). Importantly, there is significant variability in Schirmer tear test scores depending on the circumstances in which the test is conducted. This variability can occur from day to day even within the same patient. Thus, the comparison of Schirmer scores typically poses a challenge for researchers.

81. Another commonly used diagnostic device is corneal and conjunctival staining. For these tests, a stain (such as fluorescein, rose bengal, or lissamine green) is placed in the eye.

Particular stains can be used that highlight areas of poor wetting, devitalized or absent tissue on the surface of the eye, or irregular areas of the corneal surface. The stains thus enable ophthalmologists to measure the degree of a patient's dry eye problem. These tests also allow doctors to identify areas of the cornea and/or conjunctiva that have been damaged by dry eye conditions. Slit lamp examination, which permits direct examination of the ocular surface and adjacent tissues, is an essential aspect of diagnosis of dry eye conditions.

82. Another objective test performed in patients with suspected or diagnosed dry eye conditions is tear break-up time (TBUT), which measures the stability of the tear film.

83. Other measures of dry eye include subjective indicators such as a sandy or gritty feeling in the eye, ocular dryness, photophobia, blurred vision (especially when intermittent), or a burning or stinging sensation. Overall levels of patient discomfort are also often gaged.

A. The 1990s: Allergan develops Restasis.

84. Allergan has found its niche within the pharmaceutical industry as a developer and manufacturer of ophthalmic drugs. One of the company's long-term projects was the development of an effective dry eye treatment. Towards this end, Allergan began testing combinations of castor oil and cyclosporin A in the early 1990s.

1. The Kaswan Patent

85. Before Allergan could begin this research in earnest, it had to acquire an important patent in the space from another pharmaceutical company, Sandoz. U.S. Patent No. 4,839,342 (the "Kaswan patent") disclosed cyclosporine's potential as a dry eye treatment. The patent claimed methods for enhancing or restoring lacrimal gland tearing through topical administration of cyclosporine to the eye in a pharmaceutically acceptable vehicle. The Kaswan patent also recited use of castor oil, among other compounds, as a pharmaceutically acceptable vehicle for delivery of cyclosporine to the eye.

86. In 1993, Allergan bought a license from Sandoz to use that patent and commenced testing various formulations of cyclosporine.

87. One of the major challenges Allergan's scientists confronted was how to deliver cyclosporine to the eye. Cyclosporine is highly insoluble in water and therefore very difficult to deliver in an aqueous solution.

88. Allergan eventually solved this problem by developing an oil-in-water emulsion that contained a small amount of castor oil (a hydrophobic vehicle that would dissolve the cyclosporine) together with an emulsifier and an emulsion stabilizer in water.

89. Allergan disclosed this achievement in two patents.

2. The Ding I Patent

90. On December 12, 1995, the PTO issued U.S. Patent No. 5,474,979 ("the Ding I patent"). This patent disclosed Allergan's cyclosporine / castor oil emulsion. More specifically, the patent claimed a pharmaceutical emulsion consisting of between about 0.05% and about 0.4% by weight cyclosporine; between about 0.625% and about 0.4% by weight castor oil; about 1% by weight polysorbate 80 (an emulsifier); about 0.05% by weight Pemulen (an emulsion stabilizer); and about 2.2% by weight glycerin. The Ding I patent described this emulsion as having a "high comfort level and low irritation potential"[62] as well as long-term stability.[63]

91. The patent also specified four examples of the claimed invention. The table below, which appeared as Example 1 of the Ding I patent,[64] disclosed multiple potential formulations for the castor oil and cyclosporine emulsion. For example, the formulation labeled

[62] Ding I patent col. 1, ll. 8-9.

[63] *Id.* col. 3, ll. 58-63.

[64] *Id.* col. 4, ll. 31-43.

D consisted of 0.1% cyclosporine and 1.25% castor oil, while E contained 0.05% cyclosporine and 0.625% castor oil.

Example 1

	A	B	C	D	E
Cyclosporin A	0.40%	0.20%	0.20%	0.10%	0.05%
Castor oil	5.00%	5.00%	2.50%	1.25%	0.625%
Polysorbate 80	1.00%	1.00%	1.00%	1.00%	1.00%
Pemulen ®	0.05%	0.05%	0.05%	0.05%	0.05%
Glycerine	2.20%	2.20%	2.20%	2.20%	2.20%
NaOH	qs	qs	qs	qs	qs
Purified water	qs	qs	qs	qs	qs
pH	7.2–7.6	7.2–7.6	7.2–7.6	7.2–7.6	7.2–7.6

92. The Ding I patent further stated that the preferred weight ratio of cyclosporine to castor oil was below 0.16 (which is the maximum solubility level of cyclosporine in castor oil) and the more preferred weight ratio of cyclosporine to castor oil was between 0.02 and 0.12.

93. The formula Allergan eventually settled on and sold as Restasis falls within the range of values disclosed and claimed in the Ding I patent.

3. The Ding II Patent

94. On November 9, 1999, Allergan obtained a second patent related to ocular emulsions. U.S. Patent No. 5,981,607 ("the Ding II patent") claimed a method of alleviating dry-eye-related symptoms by topically applying an emulsion of a higher fatty acid glyceride, polysorbate 80, and an emulsion-stabilizing amount of Pemulen in water to the ocular tissue.[65] The Ding II patent further claimed an emulsion where the higher fatty acid glyceride was castor oil, in an amount between about 0.625% by weight and about 5% by weight.[66]

4. The Phase 2 Trial and Stevenson Paper

[65] Ding II patent, col. 9, ll. 2-7.

[66] *Id.* col. 10, ll. 4-10.

95. In the late 1990s, after Allergan filed for these patents, Allergan began clinical trials of several combinations of cyclosporine and castor oil. In the first clinical trial (the "Phase 2" study), Allergan tested four of the combinations listed in Example 1 of the Ding I patent: 0.05% cyclosporine with 0.625% castor oil; 0.1% cyclosporine with 1.25% castor oil; 0.2% cyclosporine with 2.5% castor oil; and 0.4% cyclosporine with 5% castor oil (Examples 1A, 1C, 1D, and 1E in the Ding I patent) for three months. Patients were evaluated at four, eight, and twelve weeks.

96. A number of different tests were used to measure patient improvement including rose bengal staining and Schirmer tear tests *without* anesthetic. The study also measured subjective symptoms of dry eye, such as ocular itching, burning, blurred vision, foreign body sensation, dryness, photophobia, and soreness or pain.

97. The patient population for the Phase 2 trials consisted of patients with moderate to severe dry eye with or without Sjogren's Syndrome. Importantly, at baseline, the Phase 2 patients that received the 0.1% cyclosporine / 1.25% castor oil formulation had a trend toward more severe disease compared to the patients in the 0.05% cyclosporine / 0.625 castor oil group. These differences in baseline characteristics (i.e., how severe the varying patients' dry eye disease was) confounded any comparison between the two groups.

98. The goal of the Phase 2 study was only to determine the safety, efficacy, and optimal dose of the drug. Researchers used the Phase 2 study results to settle on an appropriate dosage level for subsequent large-scale Phase 3 clinical studies. The Phase 3 studies would then be used to support Allergan's application to the FDA to market the drug.

99. A 2000 journal article by Dara Stevenson, Joseph Tauber, and Brenda L. Reis

("Stevenson") reported the results of Allergan's Phase 2 trial.[67] The Stevenson paper reported on a subset of 88 patients with moderate-to-severe dry eye disease that completed the Phase 2 trial: sixteen in a castor-oil-only control group; seventeen in the 0.05% cyclosporine group; eighteen in the 0.1% cyclosporine group; twenty in the 0.2% cyclosporine group; and seventeen in the 0.4% cyclosporine group.[68] This subset of patients – selected post hoc from the total 162 patients studied – was intended to have characteristics similar to those of the patients to be included in subsequent Phase 3 trials. Stevenson did not disclose the percentage of castor oil in each formulation, but it disclosed that the amount of castor oil increased relative to the cyclosporine present so that all of the cyclosporine in each formulation was dissolved.[69]

100. The Stevenson paper concluded that all tested concentrations significantly improved the ocular signs and symptoms of moderate-to-severe dry eye disease and mitigated dry eye disease's effects on vision-related functioning. And all formulations outperformed the castor-oil-only control group. Furthermore, the paper reported that all tested concentrations were safe and effective in increasing tearing in certain patient groups.

101. Critically, Stevenson concluded that there was *no clear dose-response relationship* between the 0.05% cyclosporine formulation and formulations containing greater amounts of cyclosporine. In other words, the drug's efficacy did not increase when more than 0.05% cyclosporine (the active ingredient) was present. Thus, the Stevenson paper concluded that the 0.1% cyclosporine formulation *did not perform* better than the 0.05% cyclosporine

[67] Dara Stevenson, Joseph Tauber, & Brenda L. Reis, *Efficacy and Safety of Cyclosporine A Ophthalmic Emulsion in the Treatment of Moderate-to-Severe Dry Eye Disease: A Dose-Ranging, Randomized Trial*, 107 Ophthalmology 967 (May 2000).

[68] *Id.* at 970.

[69] *Id.* at 968.

formulation.

102. The Stevenson paper did note, however, that the 0.1% cyclosporine formulation "produced the most consistent improvement in objective and subjective endpoints (such as superficial punctate keratitis and rose bengal staining)," while the 0.05% cyclosporine formulation "produced the most consistent improvements in patient symptoms (such as sandy/gritty feeling and ocular dryness)."[70] Therefore, Stevenson suggested "that subsequent clinical studies should focus on the cyclosporin[e] 0.05% and 0.1% formulations."[71]

5. The Phase 3 Trials and Sall Paper

103. Allergan's Phase 3 trials tested 0.1% and 0.05% formulations of cyclosporine. However, unlike the Phase 2 trials, the Phase 3 trials compared the safety and efficacy of 0.1% cyclosporine / 1.25% castor oil and 0.05% cyclosporine / 1.25% castor oil formulations to a castor-oil-only vehicle. In the Phase 2 trial, the castor oil concentrations of the 0.1% and 0.05% cyclosporine formulations were 1.25% and 0.625%, respectively.

104. Allergan conducted the two separate Phase 3 trials simultaneously: 293 patients were given a formulation containing 0.05% cyclosporine / 1.25% castor oil; 292 patients were given another containing 0.1% cyclosporine / 1.25% castor oil; and 292 were given a castor-oil-only control vehicle for 6 months. For these groups, 235 patients, 218 patients, and 218 patients, respectively, completed the trial. Thus, the completed Phase 3 trial (671 patients total) contained nearly *eight times* the number of patients in the Phase 2 trial (88 patients total).

105. Like the Phase 2 study, these Phase 3 trials measured patient improvement through a number of different tests and indicators including corneal staining and Schirmer tear

[70] *Id.* at 974.

[71] *Id.*

tests. However, the methods of conducting these tests in Phase 3 trials differed from the Phase 2 trials in crucial respects. With respect to Schirmer tests, the Schirmer tests were performed with and without anesthesia (whereas the Phase 2 studies performed the Schirmer test without anesthesia only). With respect to corneal staining, corneal staining scores were evaluated on a 0-5 point scale in Phase 3 as compared to a 0-3 point scale in Phase 2. These changes in methodologies made comparison across the Phase 2 and Phase 3 studies scientifically unsound.

106. What's more, these tests and symptoms were checked at one, three, four, and six months in the Phase 3 trials. Recall that in Phase 2, patients were checked at four, eight, and twelve weeks. Again, this difference between trials rendered comparisons between them unsound.

107. Furthermore – and critically – the patient inclusion criteria and baseline characteristics of the Phase 3 subjects differed in material respects from those enrolled in the Phase 2 trials. And in the Phase 3 trials, unlike the Phase 2 trial, the baseline characteristics of the 0.05% cyclosporine / 1.25% castor oil group indicated a trend towards more severe dry eye than the 0.1% cyclosporine / 1.25% castor oil group. These differences in baseline characteristics mitigated any improvement in the 0.05% cyclosporine group over the 0.01% group.

108. A 2000 published paper by Kenneth Sall, Dara Stevenson, and others reported the results of the Phase 3 trials ("Sall").[72] As part of the "Materials and Methods" section of the paper, Sall, et al. detailed their "Statistical Methods" to determine whether any results were "statistically significant," i.e. the result of more than chance alone.[73]

---

[72] Kenneth Sall, et al., *Two Multicenter, Randomized Studies of the Efficacy and Safety of Cyclosporine Ophthalmic Emulsion in Moderate to Severe Dry Eye Disease*, 107 Ophthalmology 631 (2000).

[73] *Id.* at 633-634.

109. This paper concluded that both cyclosporine formulations (0.1% and 0.05% cyclosporine) were more effective than the castor-oil-only vehicle in treating dry eye. Nevertheless, the castor oil vehicle also produced significant improvements over the patient's baseline, suggesting that castor oil itself was a contributing factor to the formulations' success. Once again, the paper reported *no dose-response effect* between the 0.05% cyclosporine / 1.25% castor oil formulation and the 0.1% cyclosporine / 1.25% castor oil formulation. In other words, the Sall paper found that the 0.05% cyclosporine formulation *was not superior* to the 0.1% formulation, and vice versa.

110. The Sall paper emphasized that the purpose of the two Phase 3 trials was to compare the efficacy and safety of the 0.05% and 0.1% cyclosporine formulations to the control. In other words, the purpose of these trials was *not* to compare the 0.05% cyclosporine formulation to the 0.1% cyclosporine formulation directly, but rather to compare those formulations to the *castor oil only vehicle*.

111. At three months, the paper reported a statistically significant difference between the 0.05% cyclosporine group and the patient's baseline score (scores without treatment) on the categorized Schirmer tear test with anesthesia. At six months, both the 0.05% cyclosporine group and the 0.1% cyclosporine group showed statistically significant improvements compared to the patients' baseline on that test. Sall also reported that at month 3 there was a statistically significant difference between the 0.05% cyclosporine group and the castor-oil only control, but not a statistically significant difference between the 0.05% cyclosporine group and the 0.1% group.

6. FDA Approval of Restasis

112. In February 1999, following the Phase 3 trials, Allergan filed a NDA with the FDA seeking authorization to market the 0.05% cyclosporine formulation tested in those trials.

The proposed commercial product – Restasis – would contain all of the components of that formulation, including 1.25% castor oil. Nonetheless, the FDA rejected this application, finding that Allergan failed to demonstrate the efficacy of Restasis.

113. In December 2002, the FDA approved the application. But the FDA narrowly authorized the sale of Restasis as "a topical immunomodulator indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca."[74]

114. In 2003, following approval, Allergan launched Restasis.

B. The 2000s: Allergan procures the second wave patents.

115. For over a decade following the approval of Restasis, Allergan filed a variety of patent applications attempting to claim combinations of castor oil and cyclosporine. Allergan did this notwithstanding the Ding I & II patents, which claimed the range of formulations within which Restasis fell, and the Stevenson and Sall studies, which demonstrated there were no statistical differences in outcomes between the 0.05% and 0.1% cyclosporine formulations.

1. September 2003 and August 2004: Allergan files new patent applications covering Restasis.

116. On September 15, 2003, Allergan filed a provisional application (a placeholder): U.S. Patent Application No. 60/503,137 ("the '137 application). Allergan followed up this application a year later, on August 27, 2004, with application No. 10/927,857 ("the '857 application"). These applications were directed to methods and compositions for treating dry eye by administering an emulsion composed of a hydrophobic component (such as castor oil) and a cyclosporine component of less than 0.1% by weight. The '857 application further specified that

[74] *Allergan*, 2017 WL 4803941, at *10.

the weight ratio of the cyclosporine component to the hydrophobic component should be less than 0.08. Dependent claims in the application recited a hydrophobic component, such as castor oil, in an amount greater than 0.625% of the composition. Thus, the application claimed subject matter encompassed by the Ding I patent.

2. January 2007: The PTO examiner rejects Allergan's '857 application.

117. On January 17, 2007, the PTO examiner rejected the '857 application. After Allergan withdrew a number of the application's claims, the examiner concluded that the remaining claims would have been obvious in light of Ding I. As the examiner explained, it was obvious to try a 0.05% cyclosporine / 1.25% castor oil formulation because that ratio fell within the limit range of ratios claim in the Ding I patent.

118. In response, Allergan amended the '857 application to include a claim to an emulsion of water, 1.25% castor oil, and 0.05% cyclosporine, i.e., Restasis. But the PTO examiner again rejected the application.

119. Allergan then appealed the rejection. While the appeal was pending, Allergan filed a continuation of the '857 application: U.S. Patent Application No. 11/897,177 ("the '177 application"). The '177 application was similar to the '857 application, but added claims regarding new conditions that the method was asserted to treat, including corneal graft rejection.

3. June 2009: Allergan concedes that the claims of its '857 application would have been obvious in light of Ding I.

120. Nonetheless, in June 2009, Allergan completely reversed course and conceded in writing that the '857 application was obvious in light of Ding I. And Allergan made a similar concession with respect to the '177 patent. Specifically, Allergan wrote to the PTO:

> The applicants concede that it would have been obvious to modify examples 1A-1E of the Ding reference to arrive at [the Restasis formula]. *The differences are insignificant*. One need only use the cyclosporin concentration of Example 1E (0.05%), the castor oil

> concentration of Example 1D (1.250%), and the remaining ingredients of those examples. As the examiner correctly observes, one of ordinary skill in the art "would readily envisage" such a composition, especially in view of Example 1B: having selected 0.05% as the concentration of cyclosporin, Example 1B (wherein the ratio of cyclosporin to castor oil is 0.04) teaches that the concentration of castor oil should be 1.25% (0.05% / 1.25% = 0.04). The applicants concede that in making this selection (0.05% cyclosporin and 1.25% castor oil) there would have been a reasonable expectation of success; the differences between Examples 1A-1E and Composition II are too small to believe otherwise.
>
> The formulation of Composition II is squarely within the teaching of the Ding reference, and the Office should disregard any statements by the applicants suggesting otherwise, whether in this application or in co-pending application no. 11/897,177.[75]

121. Thus, Allergan admitted that the "differences" between Restasis and the Ding I examples "[were] insignificant"; that in "select[ing]" the Restasis formula (0.05% cyclosporine and 1.25% castor oil), "there would have been a reasonable expectation of success"; the "differences between" the Ding I patent examples and the Restasis formula "are too small to believe otherwise"; and the composition claims advanced by the '857 and '177 applications were "squarely within the teaching of the Ding reference."[76] In its concession, Allergan also included a table demonstrating *exactly how* Restasis would be "readily envisage[d]" based on Examples 1B, 1D, and 1E of the Ding I patent[77]:

[75] *Id.* at *9 (quoting Allergan's concession to the PTO) (emphasis added).

[76] *Id.*

[77] *Id.* at *19.

Compositions of the Ding reference compared to

Composition II of the present application

	Ding *et al.* Example 1B	Ding *et al.* Example 1D	Ding *et al.* Example 1E	Composition II
Cyclosporin A	0.20 %	0.10 %	**0.05 %**	**0.05 %**
Castor Oil	5.00 %	**1.250 %**	0.625 %	**1.250 %**
Polysorbate 80	1.00 %	1.00 %	1.00 %	1.00 %
Pemulin®	0.05 %	0.05 %	0.05 %	0.05 %
Glycerine	2.20 %	2.20 %	2.20 %	2.20 %
NaOH	qs	Qs	qs	qs
Purified water	qs	Qs	qs	qs
pH	7.2-7.6	7.2-7.6	7.2-7.6	7.2-7.6
cyclosporin : castor oil	**0.04**	0.08	0.08	**0.04**

122. Allergan then withdrew its pending appeal and canceled all of the ’857 application’s pending claims.

123. Nonetheless, it added a new claim to the application: a composition in which the amount of cyclosporine was less than 0.05% and the ratio of cyclosporine to castor oil was less than 0.04.

124. On September 1, 2009, the examiner rejected this new claim as obvious in light of Ding I.

125. By April 2011, the PTO issued a notice of abandonment on the ’857 application to Allergan. (On December 21, 2013, the ’177 application issued as U.S. Patent No. 8,618,064, but this patent was narrowly limited to use of a cyclosporine formulation to treat corneal graft rejection).

126. Thus, by mid-2013, the only patent protecting Restasis was the Ding I patent. That patent was set to expire in May of 2014.

4. June 2013: The FDA issues a draft guidance for generic cyclosporine

ophthalmic emulsions.

127. In June 2013, with the Ding I patent's expiration date on the horizon, the FDA issued a draft guidance containing recommendations to applicants seeking to gain approval of ANDAs for generic versions of Restasis. Such guidance was consistent with long-standing practice of the FDA as a science-driven agency.

128. Neither draft nor final guidance are required for the FDA to approve an ANDA. The FDA often approves ANDAs in situations where it has issued no guidance at all, or where it has issued guidance only in draft form. But the posting of a draft guidance, and seeking comment on it, shows the FDA is well underway in evaluating the circumstances under which it would approve an ANDA for a particular product. As a result, the June 2013 issuance of the draft guidance for cyclosporine emulsion ophthalmic products was a clear signal to the drug industry that the FDA was actively considering the circumstances under which it would accept for filing, and approve, ANDAs for generic Restasis.

129. Under the June 2013 draft guidance, the FDA recommended the use of specified in vitro testing where the quality and quantity of the proposed ingredients of the generic were the same as that used for Restasis. (In vivo testing was recommended where they were not, and in other circumstances).

130. Because in vitro testing is often far less costly, time-consuming, and invasive than in vivo testing, posting of the draft guidance in June 2013 also signaled that would-be competitors to Allergan's Restasis brand product might well be in the position to gain ANDA approvals of cyclosporine ophthalmic emulsion, 0.05% products by May of 2014, i.e., upon expiration of the Ding I patent.

131. To qualify for the in vitro option for cyclosporine emulsion products pursuant to 21 CFR § 320.24(b)(6) (under which "any other approach deemed adequate by FDA to measure

bioavailability or establish bioequivalence" may be acceptable for determining the bioavailability or bioequivalence of a drug product), all of the following criteria must be met: (i) the test and reference listed drug ingredients are qualitatively and quantitatively the same; (ii) acceptable comparative physicochemical characterization of the test and reference listed drug formulations must be performed on seven separate, specified dimensions, and; (iii) acceptable comparative in vitro drug release rate tests of cyclosporine from the test and reference listed drug formulations.

132. An in vivo bioequivalence study with clinical endpoint is requested for any generic cyclosporine ophthalmic emulsion, 0.05% that has a different inactive ingredient, a difference of more than 5% in the amount of any inactive ingredient compared to that of the reference listed drug, or unacceptable data from in vitro comparative studies. The FDA pointed out that a bioequivalence study with clinical endpoints for cyclosporine ophthalmic emulsions may not be feasible or reliable due to the modest efficacy demonstrated by Restasis. For that reason, the draft guidance recommended that any sponsor electing to conduct such a study submit the study protocol for review.

133. The FDA solicited public comments on this draft guidance.

134. On August 17, 2013 – and despite the exacting and comprehensive approach that the FDA was taking to proposed cyclosporine ophthalmic emulsion products (that for in vitro testing to be adequate, both active and inactive ingredients be the same, and that there be similarity along 7 physiochemical characteristics) – Allergan submitted a lengthy comment to the agency asserting that the FDA could not approve any Restasis ANDA relying on in vitro testing. It told the FDA it should "replace the Draft Guidance with a revised guidance document that explains in vivo comparative clinical studies are required to demonstrate that a proposed generic

product is bioequivalent to" Restasis.[78]

135. Allergan caused its radical position to be echoed by comments submitted by several doctors who, unbeknownst to the FDA, had received payments from Allergan for "consulting" services and "travel and lodging," generally and specifically relating to Restasis. For example, Dr. Stephen Pflugfelder, who submitted a comment on August 8, 2013[79] critical of an in vitro bioequivalence option, received roughly $70,000 in payments from Allergan in 2013.[80] Similarly, on September 3, 2013,81 Dr. Jai G. Parekh posted a comment raising similar concern with the bioequivalence issue; neither he nor Allergan disclosed to the FDA that Allergan paid him nearly $9,000 in 2013 for his services relating to Restasis and other drugs.[82] Dr. Marc Bloomenstein's comment, posted August 15, 2013,[83] raising similar alarm, failed to disclose payments from Allergan in 2013, amounting to $47,665, all but two of which explicitly relate to Restasis.[84]

5. August 2013: Allergan renews its gambit to obtain secondary patents.

136. On the heels of the FDA's draft guidance and with the Ding I patent's expiration

[78] Letter from Richard Spivey, Sr. Vice-President Global Regulatory Affairs, Allergan, Inc., to the Food & Drug Admin. at 1, Docket No. FDA-2007-D-0369, 0.05% (Aug. 17, 2013).

[79] Letter from Stephen Pflugfelder to the Food & Drug Admin., Docket No. FDA-2007-D-0369-0236 (Aug. 9, 2013).

[80] *See* ProPublica, Dollars for Docs: Stephen C. Pflugfelder, https://projects.propublica.org/docdollars/doctors/pid/356009 (last visited Jan. 11, 2018).

[81] Letter from Jai G. Parekh to the Food & Drug Admin., Docket No. FDA-2007-D-0369 (Aug. 16, 2013).

[82] *See* ProPublica, Dollars for Docs: Jai G. Parekh, https://projects.propublica.org/docdollars/doctors/pid/37605 (last visited Jan. 11, 2018).

[83] Letter from Marc Bloomenstein to the Food & Drug Admin., Docket No. FDA-2007-D-0369-0239 (Aug. 15, 2013).

[84] *See* ProPublica, Dollars for Docs: Marc Bloomenstein, https://projects.propublica.org/docdollars/doctors/pid/25861 (last visited Jan. 11, 2018).

looming, Allergan decided to renew its attempt to obtain secondary patents on the Restasis formulation.

137. In August 2013, Allergan filed five continuation applications derived directly or indirectly from the '177 application. It filed a sixth in March 2014. These six additional applications were nearly identical to the previous failed applications with only minor variations in a few: Allergan added four sentences to three of the applications' specifications that further described the role of cyclosporine as an immunosuppressant and the conditions that may be treated with cyclosporine.

138. As the *Allergan* court would later explain in its decision invalidating the patents that resulted from these applications, "[t]he new applications were intended to protect the Restasis composition and the method of using that composition in treating dry eye and [keratoconjunctivitis sicca] after the expiration of the Ding I patent in 2014."[85]

139. But before prosecuting these new applications, Allergan had to claw back its prior concession that the Restasis formulation was obvious in light of Ding I.

140. Under patent law, "where there is a range disclosed in the prior art, and the claimed invention falls within that range, a relevant inquiry is whether there would have been a motivation to select the claimed composition from the prior art ranges."[86] In such circumstances, to overcome a rejection for obviousness, a patent application must "come forward with evidence that (1) the prior art taught away from the claimed invention; (2) there were new and unexpected results relative to the prior art; or (3) there are other pertinent secondary considerations."[87]

---

[85] *Allergan*, 2017 WL 4803941, at *10.

[86] *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1304-05 (Fed. Cir. 2015).

[87] *Id.* at 1305 (quoting *Galderma Labs., L.P. v. Tolmar, Inc.*, 737 F.3d 731, 738 (Fed. Cir. 2013)).

141. This was exactly the situation Allergan found itself: a prior art patent disclosed a finite range, and prior studies showed that there was motivation to select the Restasis formulation from that range. Therefore, to escape the inevitable conclusion of obviousness, Allergan would have to show some sort of an "unexpected result."

142. To do so, in its August 2013 PTO filings, Allergan represented that "since [the concession was filed], the Applicants have collected evidence that supports the patentability of the pending claims." Crucially, Allergan told the PTO that its reasserted claims were patentable because the Restasis formulation – 0.05% cyclosporine / 1.25% castor oil – performed far better than would be expected as compared to the 0.1% cyclosporine / 1.25 % castor oil formulation. More specifically, Allergan claimed that the Phase 2 trial revealed that the 0.1% formulation outperformed the 0.05% cyclosporine formulation, while the Phase 3 study revealed the 0.05% formulation outperformed the 0.1% formulation. Thus, the results of the Phase 3 trial were unexpected in light of the Phase 2 results.

143. Allergan's representations were false.

144. The outcomes used to compare different formulations – published 13 years earlier in the Stevenson and Sall papers (three years before the second wave patents' priority date) – bore out none of Allergan's claims. The Stevenson and Sall papers both concluded that there was *no dose-response effect* between the 0.05% cyclosporine and the 0.1% cyclosporine castor oil formulations. *Neither* trial showed a scientifically significant difference between the two formulations: the Phase 2 trial did not suggest the 0.1% cyclosporine formulation was superior, and the Phase 3 study did not suggest the 0.05% cyclosporine formulation was superior.

145. The *Allergan* court later explained this reality in painstaking detail in its opinion invalidating the second wave patents.

146. As the Court summarized, the Phase 2 data presented in Stevenson reported results on fourteen efficacy measures: rose bengal staining (temporal), rose bengal staining (nasal), corneal staining, Schirmer scores without anesthesia, tear film debris, tear break-up time, artificial tear use, OSDI score, stinging or burning, itching, sandy or gritty feeling, dryness, light sensitivity, and pain. For most of these efficacy measures, observations were recorded at five different points in time: week four, week eight, week twelve, post-treatment week two, and post-treatment week four. All told, there were a total of 58 data points (i.e., measurements of a particular parameter at a particular time point).

147. Accurate analysis of this data revealed that the 0.05% cyclosporine / 0.625% castor oil and 0.1% cyclosporine / 1.25% castor oil formulations were statistically significantly different for only *2 of the 58* measured data points, neither of which involved Schirmer scores. As the *Allergan* court concluded, "those two individual points of statistical significance, out of all of the tested categories and time points, are [in]sufficient to demonstrate a real difference in effectiveness between the 0.05% and 0.1% cyclosporin[e] formulations."[88]

148. As for the Phase 3 studies, twenty-one efficacy measures were observed: corneal staining, temporal conjunctival staining, nasal conjunctival staining, the sum of temporal and nasal conjunctival staining, the sum of corneal and conjunctival staining, raw Schirmer scores with anesthesia, categorized Schirmer scores with anesthesia, raw Schirmer scores without anesthesia, categorized Schirmer scores without anesthesia, OSDI score, facial expression subjective rating scale, stinging or burning, itching, sandy or gritty feeling, blurred vision, dryness, light sensitivity, pain, global evaluation of response to treatment, treatment success, and artificial tear use. Most of these efficacy markers were measured at four points: one month, three

[88] *Allergan*, 2017 WL 4803941, at *26.

months, four months, and six months. There were a total of eighty data points measured in the Phase 3 trials.

149. For these trials, at least seventy-one of the eighty total data points showed no statistically significant difference between the two cyclosporine formulations. Thus, as the *Allergan* court concluded, "the overwhelming bulk of the data (71 out of 80 data points) supports an inference that the two cyclosporin[e] formulations performed similarly, and an even larger portion of the data (76 out of 80 data points) supports an inference that the 0.05% cyclosporin[e] formulation did not perform better than the 0.1% cyclosporin[e] formulation."[89]

150. The Court summarized, "there is a dearth of evidence showing any real difference between the efficacy of the 0.05% and 0.1% cyclosporin[e] formulations in Phase 2, as presented in Stevenson, and in Phase 3, as presented in Sall. A person of skill reviewing those papers would come to the conclusion that neither formulation was more effective than the other in Phase 2. That person of skill would reach the same conclusion for Phase 3."[90]

151. In short, the Phase 2 study did not suggest the 0.1% cyclosporine formulation was superior to the 0.05% cyclosporine formulation, and the Phase 3 study did not suggest that that the 0.05% formulation was superior to the 0.1% formulation in Phase 3. The basis for Allergan's claim to patentability – that the Phase 2 trial favored the 0.1% formulation, and then the Phase 3 trial *unexpectedly* favored the 0.05% formulation – is not born out by the results of either the Phase 2 trial or the Phase 3 trial.

152. Allergan was aware of this reality and even admitted it to the FDA when Allergan initially presented the results of the Phase 3 trial to the agency: "Upon presenting the Phase 3

[89] *Id.* at *33.

[90] *Id.* at *36.

results to the FDA, Allergan explained that the performance of the 0.05% cyclosporine formulation was not surprising because the lack of a dose response – i.e., the similar level of efficacy for formulations containing 0.05% or more of cyclosporine – was observed earlier in Phase 2."[91] In fact, Allergan had initially decided to test the 0.05% formulation in the Phase 3 study because the FDA had suggested that formulation given the lack of dose response above 0.05% cyclosporin in Phase 2: *"[b]ecause we did not show a clear differentiation in effect among the doses [in Phase 2]*, it was recommended [by the FDA] that we include a lower concentration [0.05% cyclosporin] in one Phase 3 clinical trial to confirm that we have chosen the lowest effective concentration."[92]

153. The *Allergan* court further pointed out that Allergan's attempt to contort the Phase 2 trial into a study of the comparative efficacy of the 0.05% and 0.1% cyclosporine formulations, in-and-of-itself, constitutes a fundamental flaw. As explained earlier, it was *the Phase 3 studies*, not the *Phase 2 study*, that were intended to aid selection between the 0.05% and 0.1% cyclosporin formulations. With only 88 participants, the Phase 2 study was not designed to reveal statistically significant differences between the various tested formulations. As the *Allergan* court observed, "[t]he small size of the Phase 2 study makes it difficult to draw reliable conclusions about the relative efficacy of different formulations."[93] Accordingly, Allergan's effort to convert the Phase 2 study into an assessment of the relative efficacy of the 0.05% and 0.1% cyclosporine formulations in order to contrast it with the Phase 3 study "lies at the heart of the problem with its 'unexpected results' analysis."[94] Allergan should never have relied on this

[91] *Id.* at *29.

[92] *Id.* at *30 (alterations in original) (quoting Allergan's acknowledgement to the FDA).

[93] *Id.* at *23.

[94] *Id.* at *23.

study to assert the 0.1% formulation performed better than the 0.05% formulation in the first place.

154. Because Ding I disclosed the narrow range of formulations within which Restasis falls, Allergan could only escape a conclusion of obviousness by showing unexpected results. But the Phase 2 testing was neither designed to show, nor suggested, that the 0.1% formulation was superior to the 0.05% formulation. And the Phase 3 study similarly failed to show a dose response or preferential efficacy between dosages. Furthermore, the Phase 2 and Phase 3 trial could not properly be compared to each other. As previously explained, these trials had disparate patient populations, testing methodologies, and measured results at different points in time. Allergan's own conclusion – 13 years earlier – that there was nothing unexpected in the Phase 3 results, was the truth. Allergan's later representations to the contrary were false.

155. Between October 10 and 17, 2013, the patent examiner rejected at least four of Allergan's second wave patent applications, once again relying heavily on the Ding I patent.

6. October 14, October 23, and December 5, 2013: Allergan submits a highly misleading declaration – the Schiffman declaration – to overcome the examiner's rejection.

156. On October 14, October 23, and December 5, 2013, Allergan submitted a declaration from Dr. Rhett M. Schiffman claiming that test results showed the Restasis formulation (0.05% cyclosporine / 1.25% castor oil) produced new and unexpected results relative to the 0.05% cyclosporine / 0.625% castor oil and 0.1% cyclosporine / 1.25% castor oil formulations recited in the Ding I patent.[95] Specifically, Allergan relied on Dr. Schiffman's declaration to claim:

> [S]urprisingly, the claimed formulation [of 0.05% cyclosporin and

[95] Allergan submitted this declaration in four of the six patent applications on October 14 and 23, 2013. It submitted this declaration in the fifth patent application on December 5, 2013.

> 1.25% castor oil] demonstrated an 8-fold increase in relative efficacy for the Schirmer Tear Test score in the first study of Allergan's Phase 3 trials compared to the relative efficacy for the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation discussed in Example 1E of Ding, tested in Phase 2 trials. . . . [T]he claimed formulations also demonstrated a 4-fold improvement in the relative efficacy for the Schirmer Tear Test score for the second study of Phase 3 and a 4-fold increase in relative efficacy for decrease in corneal staining score in both of the Phase 3 studies compared to the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation tested in Phase 2 and disclosed in Ding (Ding 1E). *This was clearly a very surprising and unexpected result*.[96]

In plain English, Dr. Schiffman declared that the Schirmer tear test scores for the 0.05% cyclosporine / 1.25% castor oil formulation (Restasis) in the first Phase 3 trial revealed that 0.05% cyclosporine formulation resulted in an *8-fold* increase in efficacy over the 0.05% cyclosporine / 0.625% castor oil formulation tested in the Phase 2 trial (and disclosed in Ding I). Dr. Schiffman further claimed, based on the Schirmer tear test scores in the second Phase 3 trial and the corneal staining tests results in both Phase 3 trials, that the Restasis formulation showed a *4-fold* improvement over the 0.05% cyclosporine / 0.625% castor oil formulation tested in Phase 2. According to Allergan and Dr. Schiffman, these results were surprising because the Phase 2 trial had suggested the 0.1% cyclosporine formulation was superior to the 0.05% formulation.

157. Dr. Schiffman's representations to the PTO were false and misleading. As the *Allergan* court explained in its invalidity decision, Dr. Schiffman's declaration is unreliable as a basis for patentability for four principal reasons:

- *First*, Dr. Schiffman relied on statistically insignificant outcomes. Allergan's *own statistical analyses* had shown that there were no statistically significant differences in outcomes between formulations. Nonetheless, Schiffman

[96] *Id.* at * 11 (second alteration in original) (quoting Allergan's representation of Dr. Schiffman's declaration to the PTO).

concealed the lack of statistical significance from the PTO. Scientists do not rely on statistically insignificant results, and scientists would not rely on the analytic manipulations Schiffman performed.

- *Second*, Dr. Schiffman did not compare like test results. Schiffman compared the results of Schirmer tear tests performed *with* anesthetic to Schirmer tear tests conducted *without* anesthetic. He also compared corneal staining scores graded on a 0-3 point scale to those graded on a 0-5 point scale. Furthermore, the Phase 2 and Phase 3 trials examined different patient populations (the baseline characteristics of the patient populations materially differed); measured different time points (in Phase 2, patients were evaluated at four, eight, and twelve weeks, whereas, in Phase 3, patient were evaluated at one, three, four, and six months); and tested different formulations (Phase 2 tested 0.1 % cyclosporine / 1.25% castor oil and 0.05% cyclosporine / 0.625% castor oil, while Phase 3 tested 0.1% cyclosporine / 1.25% castor oil and 0.05% cyclosporine / 1.25% castor oil). Thus, comparisons between the Phase 2 and Phase 3 trials have no scientific value.

- *Third*, Dr. Schiffman used data manipulation techniques to amplify small differences between test results. For example, he relied on median changes from baseline in order to create an illusion of improved efficacy. He then relied on a faulty "ratio-of-ratios" technique to misleadingly enhance differences between results. Such contortions gave the PTO the false impression that Dr. Schiffman had actually obtained significant results.

- *Fourth*, Dr. Schiffman failed to tell the PTO that he lifted the data he presented from the Sall paper. Thus, his data was not only over a decade old, it was also *prior art* to the second wave Restasis patents. As such, this data could not support Allergan's second wave patent applications.

In short, as the *Allergan* court concluded, "Dr. Schiffman's declaration and the accompanying exhibits[] painted a false picture."[97]

a. Dr. Schiffman relied on statistically insignificant outcomes.

158. First, Dr. Schiffman improperly relied on statistically insignificant data to draw his desired conclusions: he disregarded the error bars and p-values associated with the data he lifted from the Sall study.

159. A p-value is the probability that a given outcome is result of random chance. P-

[97] *Id.* at *39.

values are critical because they tell scientists whether a given result is likely real. If the P-value is small enough (e.g., less than 0.05), then the result is "statistically significant." P-values are calculated through head-to-head comparisons (pair-wise comparison) of the mean values of two groups of data. For example, one could compare (a) the mean improvement in Schirmer scores over a three-month period for patients treated with the 0.05% cyclosporine formulation to (b) the mean improvement in Schirmer scores over a three-month period for patients treated with the 0.1% cyclosporine formulation. A pair-wise comparison of those two means could be used to derive a p-value indicating whether there was a real difference between the average improvement in Schirmer scores for the 0.05% cyclosporine formulation and the average improvement in Schirmer scores for the 0.1% cyclosporine formulation. A small p-value, such as p = 0.03, would indicate that the observed difference between those averages is likely real, in that the difference observed could be the result of random chance only 3% of the time. A large p-value, such as p = 0.30, would mean that the difference as large or larger than the one observed is the result of random chance 30% of the time. Scientists typically regard a p-value of 0.05 as the cut off for statistical significance: data with p-values much higher than 0.05 are disregarded.

160. Dr. Schiffman omitted the p-values and standard error bars associated with the data outcomes he took from the Sall paper in an attempt to pass off statistically insignificant differences between the 0.05% and 0.1% cyclosporine formulations as important. In reality, and as the *Allergan* court explained, "none of the pair-wise comparisons between the two cyclosporin formulations for corneal staining and Schirmer scores in the Phase 2 study or the pooled Phase 3 studies demonstrated statistical significance at any time point."[98]

161. In fact, many of the p-values for the pair-wise comparisons were very high. For

[98] *Id.* at *37.

example, the p-values for a comparison of Schirmer scores without anesthesia in Phase 2 – the only p-value regarding Schirmer scores that were calculated in Phase 2 – was 0.651 at week 4, 0.790 at week 8, and 0.834 at week 12. No scientist would take seriously the differences in the raw data results between the two cyclosporine formulations given these extremely high p-values. These p-value essentially communicated that any measured difference in the efficacy of the two formulations was more likely-than-not a result of random chance. Interpreted properly, the data Schiffman told the PTO showed "unexpected results" actually showed no significant difference in efficacy between the 0.05% and 0.1% formulation.[99]

162. When Dr. Schiffman was questioned about this misrepresentation during the second wave patents' validity trial, all he could muster was: "I think we're making – in a sense, we're trying to make too much out of statistical techniques when the bigger picture is – is – is really sufficient, I think."[100]

163. As the *Allergan* court explained, "statistical significance is an important component in establishing the reliability of the clinical data for a person of skill in the art."[101] Allergan recognized this fact by creating a detailed statistical plan prior to executing the Phase 2 and Phase 3 studies, as set forth in the Restasis NDA and as reported in Stevenson and Sall. Indeed, the lack of statistical significance between the two formulations is what kept Stevenson, et al., from concluding, in their peer-reviewed paper, that the 0.1% formulation did best or that the 0.1% formulation did better than the 0.05%. As Allergan's expert conceded at trial, "one point of peer review is to make sure that authors don't overstate their case."[102]

---

[99] *Id.* at *64.

[100] *Id.* at *28.

[101] *Id.* at *29.

[102] *Id.*

b. Dr. Schiffman did not compare like test results.

164. Second, in addition to Dr. Schiffman's deliberate concealment of the p-values associated with the data he presented, Dr. Schiffman did not disclose to the PTO that the Phase 2 and 3 test results he compared to demonstrate that the 0.05% cyclosporine formulation performed better than the 0.1% formulation in Phase 3 *came from two distinct types of Schirmer tests*. In his declaration, Dr. Schiffman compared test scores from Schirmer tests performed *without* anesthesia in Phase 2 to Schirmer tests performed *with* anesthesia in one of the two Phase 3 studies. Schirmer tear testing *with* anesthesia measures the baseline level of tearing; Schirmer tear testing *without* anesthesia measures baseline tearing plus some level of reflective tearing based on the patient's reaction to the filter paper used to give the test. Therefore, Schirmer tear tests *without* anesthesia will inherently measure more tearing than Schirmer tear testing *with* anesthesia. Thus, comparing a Schirmer tear test *without* anesthesia to one *with* anesthesia is akin to comparing the marathon time of a runner who ran an easy course in good conditions to the time of a runner on a harder course with worse conditions to determine the faster runner. In reality, the Schirmer tear test results *without* anesthesia in Phase 3 showed a trend similar to the Schirmer tear test results *without* anesthesia in Phase 2 in that both favored the 0.1% cyclosporine formulation, not the 0.05% cyclosporine formulation. But neither Schiffman nor Allergan disclosed this fact to the PTO.

165. Instead, Schiffman's declaration included only an evaluation of the Schirmer tear test results with anesthesia in Phase 3, using medians, which spuriously seemed to favor the 0.05% cyclosporine formulation. Relying on his cherry-picked comparison, Schiffman told the PTO that 0.05% cyclosporine formulation (the Restasis formulation) "demonstrated an *8-fold* increase in relative efficacy" as compared to the 0.1% formulation. Only through his manipulation of the data – comparing the results of two different types of dry eye test – was Dr.

Schiffman able to suggest that the 0.05% cyclosporine / 1.25% castor oil formulation tested in Phase 3 was 8 times more effective than the 0.05% cyclosporine / 0.625% castor oil or 0.1% cyclosporine / 1.25% castor oil castor oil formulations in Phase 2. A scientifically sound comparison of the data showed no such increase in efficacy.

166. Schiffman also declined to disclose that the Phase 2 and Phase 3 trials evaluated corneal staining scores on different scales: in Phase 2, corneal staining scores were evaluated on a 0-3 scale, whereas the Phase 3 studies used a 0-5 point scale. This difference in methodology rendered Schiffman's comparisons of corneal staining scores across the trials scientifically inappropriate.

167. Furthermore, Schiffman did not disclose to the PTO that the baseline characteristics of the patient populations in the Phase 2 and Phase 3 studies materially differed. These differences confounded any comparison across the trials, but Schiffman kept this information a secret. He further did not disclose that the differences in formulations and time points measured across the Phase 2 and 3 clinical trials rendered his analysis inappropriate.

c. Dr. Schiffman relied on medians and used a "ratio of ratios" data analysis technique that exaggerated the differences in test results.

168. Third, the data and method that Dr. Schiffman used to calculate the differences in efficacy between the formulations overstated the differences between them.

169. Dr. Schiffman's statement that the Restasis formulation tested in the first Phase 3 study led to an "8-fold improvement" over the 0.05% cyclosporine / 0.625% castor oil formulation tested in Phase 2 was based on a misleading "ratio-of-ratios" calculation. Dr. Schiffman first compared patients' median change from baseline in Schirmer test scores at week 12 for the 0.05% and 0.1% cyclosporine formulations in the Phase 2 study. He calculated that the change from baseline for the 0.05% formulation was approximately one-quarter as large as the

change from baseline for the 0.1% formulation. He then conducted a similar comparison of the 0.05% and 0.1% formulations in Phase 2 with regard to the median change in corneal staining score, again concluding that the change from baseline was approximately one-quarter as large for the 0.05% formulation as for the 0.1% formulation. He then performed the same calculation for corneal staining and Schirmer scores without anesthesia for each of the two Phase 3 studies. The mean improvement in the corneal staining scores for both Phase 3 studies was the same, as was the mean improvement in the Schirmer scores for the second Phase 3 study. However, Dr. Schiffman calculated the improvement in Schirmer scores for the first Phase 3 study as being twice as great for the 0.05% formulation as for the 0.1% formulation. He did so by: (1) ignoring all of the mean Phase 3 Schirmer data, (2) ignoring *eleven* of *twelve* Phase 3 median Schirmer data points that either showed no difference between the formulations or *favored* the 0.1% formulation, and (3) cherry-picking the *one* median Phase 3 Schirmer data point that supported his "surprising result" conclusion. He performed similar data manipulation for the corneal staining scores.

170. As the *Allergan* court explained, Dr. Schiffman's calculations were "misleading" because they were based on a calculation *of the ratio of the differences* between the improvement from baseline for the 0.05% and 0.1% cyclosporine formulations for the two studies. Even though the actual difference in the median improvement in Schirmer scores for the 0.05% and 0.1% formulations in Phase 2 was only about 1.5 millimeters, the use of ratios of medians to represent the difference suggested that the difference was 4:1 in favor of the 0.1% formulation. Similarly, although the difference between the 0.05% and 0.1% formulations in the first study of Phase 3 Schirmer scores was not dramatic, depicting that difference as a ratio of the medians of change from baseline tended to exaggerate its significance by suggesting that the 0.05%

formulation was twice as effective as the 0.1% formulation. Dr. Schiffman then calculated *the ratio of the two ratios* (2/.25), deriving a ratio of 8:1, which grossly misrepresented the difference between the 0.05% and 0.1% formulations as measured in the Phase 2 and Phase 3, suggesting that the 0.05% cyclosporine / 1.25% castor oil formulation performed eight times as well in the first study of Phase 3 as the 0.05% cyclosporine / 0.625% castor oil formulation in the Phase 2 study.

171. The *Allergan* court provided a useful example that helps show why such a ratio-of-ratios calculation is misleading:

> Suppose that the baseline value on some metric was 10.00. Suppose further that the Phase 2 data showed an improvement to 10.01 for the 0.05% cyclosporin/0.625% castor oil formulation and an improvement to 10.03 for the 0.1% cyclosporin/1.25% castor oil formulation. Suppose further that the Phase 3 data showed an improvement to 10.01 for the 0.1% cyclosporin/1.25% castor oil formulation and an improvement to 10.03 for the 0.05%/1.25% castor oil cyclosporin formulation. Finally, suppose that statistical analysis showed that none of those small variations in performance were statistically significant, but were likely just the product of experimental noise. Nonetheless, the ratio of the measured improvements in the metric for the 0.1% cyclosporin/1.25% castor oil formulation to the 0.05% cyclosporin/0.625% castor oil formulation in Phase 2 would [be] 3:1, and the ratio of the measured improvements in the metric for the 0.1% cyclosporin/1.25% castor oil formulation to the 0.05% cyclosporin/1.25% castor oil formulation in Phase 3 would be 1:3. The ratio of those two ratios would be 9:1. Any conclusion from the "ratio of ratios" that there was a nine-fold relative improvement in performance by the 0.05% formulation in Phase 3 over Phase 2 would obviously be spurious.[103]

172. Dr. Schiffman's calculations also ignored and hid the fact that the subset of Phase 2 patients he analyzed contained a small number of patients and that the difference in the means for the 0.05% cyclosporine formulation compared to the 0.1% formulation on some metrics,

[103] *Id.* at *38.

including Schirmer scores, were not statistically significant.

173. Furthermore, Dr. Schiffman cherry-picked the outcomes of tests to compare the performance of the 0.05% and 0.1% cyclosporine formulations. In other test categories for the Phase 2 studies, the 0.05% formulation did better than the 0.1% formulation. As the *Allergan* court explained, "[i]n order to make an appropriate assessment of the Phase 2 study data, it is necessary to view that data globally, not to select the data points that are most favorable to a particular desired outcome."[104]

174. Finally, Dr. Schiffman relied on *median* data, which are refractory to meaningful statistical analysis and therefore are rarely used in reporting Phase 2 and Phase 3 clinical trials results, instead of relying on mean data, which are the normal way such results are analyzed and reported. In doing so, Schiffman rejected Allergan's own statistical analysis, showing no meaningful difference between the 0.05% and 0.1% formulations.

175. In sum, by using ratios of ratios of medians of differences, Dr. Schiffman manipulated the raw data outcomes to create the illusion that 0.05% (Restasis) formulation was far more effective in the Phase 3 study than it was in the Phase 2 study. Put another way, Dr. Schiffman convinced the PTO that Allergan had achieved an unexpected result through a highly misleading interpretation of the data.

d. Dr. Schiffman concealed the fact that the data he relied on was over a decade old; prior art to the second wave patents.

176. Fourth and finally, Dr. Schiffman's declaration failed to inform the PTO that the outcomes he relied on in his declaration had been published *thirteen years before* the second wave patent applications and *three years before* their priority dates. Thus, as the Eastern District

[104] *Id.* at *39.

of Texas noted, a "major flaw in Dr. Schiffman's presentation was [] that, *even if* the results reported in Sall would have been surprising at the time the Phase 3 trials were conducted, those results *were publicly known before the invention*."[105] In other words, the results published in the Sall paper were prior art to the second wave patents applications and could not serve as a basis for their patentability.

177. Had Allergan made clear to the PTO examiner that Dr. Schiffman's declaration was based on data lifted from prior art known to Allergan for over a decade, as Allergan's duty of disclosure, candor, and good faith required, the PTO examiner would have rejected all of the second wave applications for the same reasons it had denied every other prior application: the claims presented were obvious in light of the prior art.

178. Based on these serious problems, the Allergan court would later conclude that Dr. Schiffman's "presentation to the PTO substantially overstated the difference between the clinical results obtained with the Ding formulations and the clinical results obtained with the Restasis formulation."[106] As the court explained:

> To the extent that Allergan relies on Dr. Schiffman's presentation to the PTO . . . and the fact that the examiner concluded that unexpected results had been shown . . . the Court finds that the presentation made to the examiner in 2013, including Dr. Schiffman's declaration and the accompanying exhibits, *painted a false picture* of the comparative results of the Phase 2 and Phase 3 trials. In addition, that presentation *created the misleading perception* that the evidence that Dr. Schiffman relied on to show unexpected results was not known at the time of the invention.[107]

179. The *Allergan* court would also later conclude that "the examiner's finding of

[105] *Id.* (emphasis added).

[106] *Id.* at *64.

[107] *Id.* at *39.

unexpected results . . . was [based] on evidence that did *not accurately depict* the comparative results of the two Allergan studies and that was, in any event, disclosed in the prior art."[108] In other words, but for Allergan submission of Dr. Schiffman's highly misleading declaration, the PTO would never have issued the patent.

7. October 14 and 23, 2013: Allergan submits a second, highly misleading declaration – the Attar declaration – to overcome the examiner's rejection.

180. In addition to the Schiffman declaration, Allergan submitted a second, fraudulent declaration from Dr. Mayssa Attar. Like Schiffman, Dr. Attar falsely claimed that the Restasis formulation led to "unexpected results." Dr. Attar stated that she read Dr. Schiffman's declaration and agreed with his statements. In vouching for Schiffman's fraudulent declaration, Dr. Attar herself misled the PTO.

181. Dr. Attar also misleadingly construed certain pharmacokinetic studies conducted on animal eyes in her declaration. Her interpretation of these studies relied on many of the same data manipulation techniques as Dr. Schiffman's declaration and was highly misleading for similar reasons.

182. For example, Dr. Attar failed to disclose that a key diagram in her declaration, Exhibit B, compared incomparable results from two different studies with different methodologies and purposes, and the diagram appeared in neither study.

183. Nor did she make clear that the results of these studies had never been published and would not have informed the views of a person of ordinary skill in the art.

184. Her declaration also misconstrued basic pharmaceutical principles. It stated that:

> Generally speaking, it was understood that pharmacokinetic/pharmacodynamic relationship would indicate

[108] *Id.* (emphasis added).

> that as more cyclosporin A reaches the target tissues of the ocular surface, such as the cornea and conjunctiva, the more immunomodulatory and more anti-inflammatory activity that can take place and the more therapeutically effective a drug can be in treating dry eye.

185. Basic drug science dictates otherwise. Most pharmaceutical ingredients can reach a plateau of therapeutic efficacy: on the plateau, addition of more active ingredient does not cause more therapeutic effect. Dr. Attar never addressed whether the formulations she compared had reached the therapeutic plateau and concealed that the Phase 2 and Phase 3 trials suggested that the 0.1% and 0.05% cyclosporine formulations had.

8. November 21, 2013: The Schiffman and Attar declarations convince the PTO examiner to allow the second wave patents.

186. The Schiffman and Attar declarations had their intended effect. On November 21, 2013, the examiner reversed course and allowed the second wave patent claims. Trusting Dr. Schiffman, Dr. Attar, and Allergan not to misrepresent the truth – as their duties of candor and good faith required – the PTO examiner did not uncover the manipulations, false comparisons, and misrepresentations that these declarations contained.

187. Instead, the examiner concluded that the Schiffman declaration

> [i]s deemed sufficient to overcome the rejection . . . because: After carefully reviewing exhibits A-F, which compare the instantly claimed embodiment having 0.05%/1.25% castor oil with embodiments E and F of Ding et al. (0.10%/1.25% [cyclosporin/]castor oil and 0.05%/.625% cyclosporin/castor oil ratios), Examiner is persuaded that, *unexpectedly, the claimed formulation (0.05% cyclosporin A/1.25% castor oil) demonstrated an 8-fold increase in relative efficacy* for the Schirmer Tear Test score in the first study of Phase 3 trials compared to the relative efficacy for the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation disclosed in Example 1E of Ding, tested in Phase 2 trials. . . .
>
> Exhibits E and F also illustrate that the claimed formulations comprising 0.05% cyclosporin A/1.25% castor oil also *demonstrated a 4-fold improvement in the relative efficacy* for the

> Schirmer Tear Test score for the second study of Phase 3 and *a 4-fold increase in relative efficacy* for decrease in corneal staining score in both of the Phase 3 studies compared to the 0.05% by weight cyclosporin A/0.625% by weight castor oil formulation tested in Phase 2 and disclosed in Ding (Ding 1E).[109]

188. Thus, the examiner allowed the second wave Restasis patents *based on* Dr. Schiffman's declaration. The examiner believed Allergan's representation that the Restasis formulation demonstrated 8- and 4-fold increases in efficacy over the 0.05% cyclosporine / 0.625% castor oil formulation tested in the Phase 2 trial.

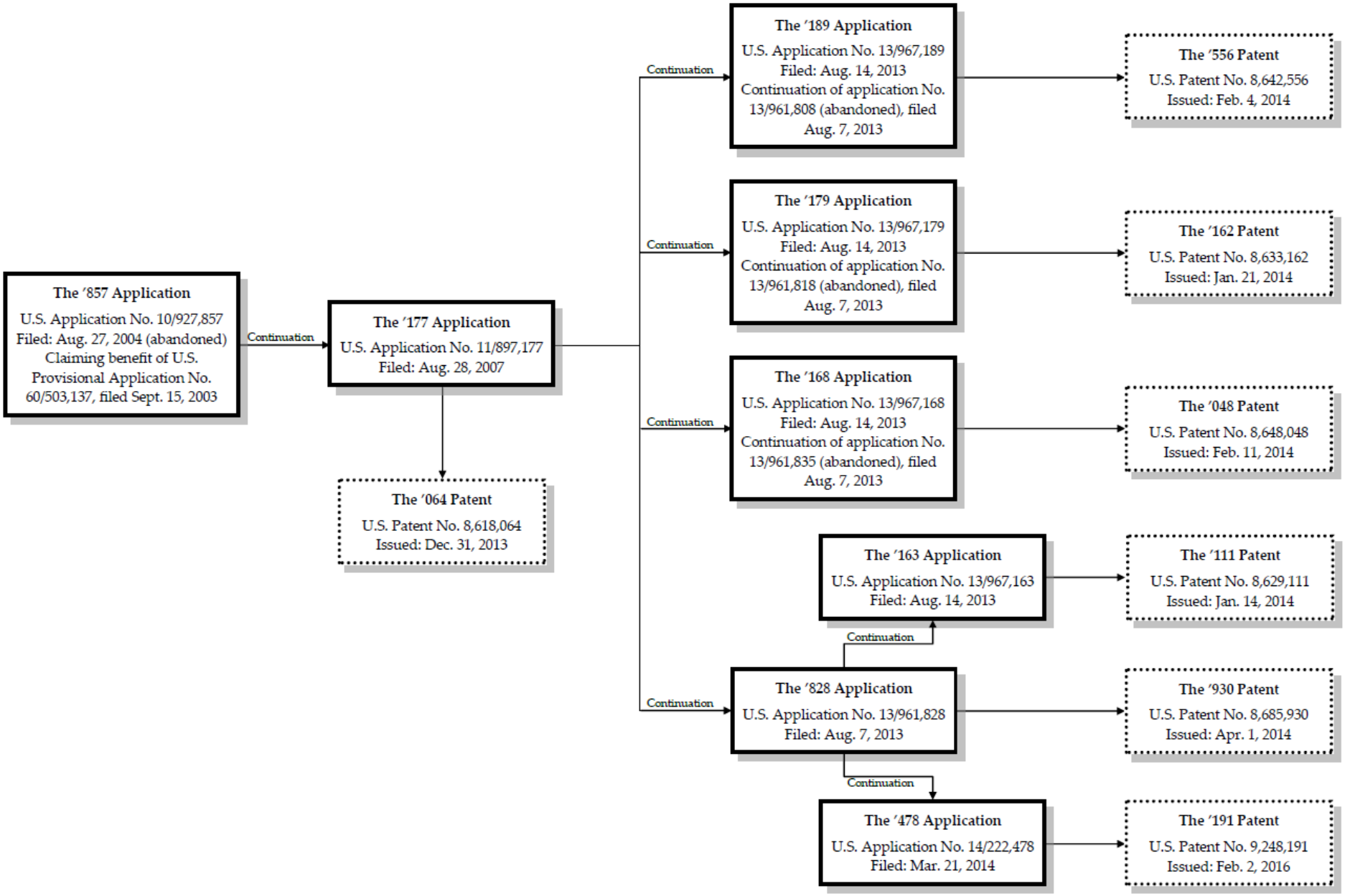
189. The examiner also deemed the Attar declaration sufficient to overcome the prior obviousness rejection.

190. But for these declarations, the examiner would not have issued the new Restasis patents. Indeed, during the trial of the second wave patents' validity, Dr. Schiffman conceded that his declaration was instrumental in persuading the PTO to grant the second wave applications.[110]

191. In January through April 2014, five of the applications issued as second wave patents: U.S. Patent Nos. 8,629,111 ("the '111 patent"), 8,633,162 ("the '162 patent"), 8,642,556 ("the '556 patent"), 8,648,048 ("the '048 patent"), and 8,685,930 ("the '930 patent"). A sixth would issue in February 2016 as U.S. Patent No. 9,248,191 ("the '191 patent"). The figure below summarizes these patents and their lineage.

[109] *Id.* at *11 (alterations in original except for the first).

[110] *Id.* at *20.


The '857 Application
U.S. Application No. 10/927,857
Filed: Aug. 27, 2004 (abandoned)
Claiming benefit of U.S. Provisional Application No. 60/503,137, filed Sept. 15, 2003
Continuation
The '177 Application
U.S. Application No. 11/897,177
Filed: Aug. 28, 2007
The '064 Patent
U.S. Patent No. 8,618,064
Issued: Dec. 31, 2013
Continuation
The '189 Application
U.S. Application No. 13/967,189
Filed: Aug. 14, 2013
Continuation of application No. 13/961,808 (abandoned), filed Aug. 7, 2013
The '556 Patent
U.S. Patent No. 8,642,556
Issued: Feb. 4, 2014
Continuation
The '179 Application
U.S. Application No. 13/967,179
Filed: Aug. 14, 2013
Continuation of application No. 13/961,818 (abandoned), filed Aug. 7, 2013
The '162 Patent
U.S. Patent No. 8,633,162
Issued: Jan. 21, 2014
Continuation
The '168 Application
U.S. Application No. 13/967,168
Filed: Aug. 14, 2013
Continuation of application No. 13/961,835 (abandoned), filed Aug. 7, 2013
The '048 Patent
U.S. Patent No. 8,648,048
Issued: Feb. 11, 2014
The '163 Application
U.S. Application No. 13/967,163
Filed: Aug. 14, 2013
The '111 Patent
U.S. Patent No. 8,629,111
Issued: Jan. 14, 2014
Continuation
Continuation
The '828 Application
U.S. Application No. 13/961,828
Filed: Aug. 7, 2013
The '930 Patent
U.S. Patent No. 8,685,930
Issued: Apr. 1, 2014
Continuation
The '478 Application
U.S. Application No. 14/222,478
Filed: Mar. 21, 2014
The '191 Patent
U.S. Patent No. 9,248,191
Issued: Feb. 2, 2016

192. In sum, Allergan procured the second wave patents through knowing, intentional fraud on the PTO.

C. Early 2014: Allergan wrongfully lists its second wave patents in the Orange Book.

193. After acquiring the second wave patents through fraud, Allergan employed another tactic to frustrate the introduction of generic Restasis products: it listed the second wave patents in the Orange Book.[111]

194. Throughout the first quarter of 2014, Allergan listed every second wave patent it obtained in the Orange Book:

Patent Number	Date of Orange Book listing
8,629,111 (the '111 patent)	January 14, 2014
8633,162 (the '162 patent)	January 21, 2014
8,642,556 (the '556 patent)	February 4, 2014
8,648,048 (the '048 patent)	February 11, 2014
8,685,930 (the '930 patent)	April 1, 2014

195. Each of Allergan's listings was wrongful.

196. Under the Hatch-Waxman Amendments, an NDA holder may only submit patent information to the FDA for listing in the Orange Book if the patent is one for which "a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug."[112]

197. None of the second wave patents could "reasonably be asserted" against any applicants for generic Restasis. First, the second wave patents were knowingly acquired by fraud

[111] Drug manufacturers send their drug patent information to the FDA, which then lists the patents in the Orange Book. Therefore, the drug manufacturers themselves do not technically list the patents; the FDA does. However, for simplicity's sake, this complaint refers to such listings as drug-manufacturer listings since the drug manufacturers are the actors that cause the patents to be listed.

[112] 21 U.S.C. § 355(b)(1), (c)(2).

on the PTO. Second, in the context of litigation to enforce any one of the second wave patents, no reasonable litigant would realistically expect to prevail on the merits of the litigation; the obviousness of the patents would be revealed, as would the falsity of Allergan's assertion of surprising comparative efficacy of the 0.05% formulation as of the priority date of September 2003. As a result, Allergan could not "reasonably" assert the second wave patents against a would-be generic competitor, as Allergan harbored no realistic ability to prevail on the merits of such litigation.

198. Allergan knew that the second wave patents were not eligible for listing in the Orange Book: it knew Dr. Schiffman's declaration constituted a misrepresentation. And it knew the second wave patents would be declared invalid as obvious given the absence of any true, surprising efficacy of the 0.05% formulation as of the priority date of September 2003.

199. By listing the second wave patents in the Orange Book, Allergan imposed additional regulatory requirements on existing and future Restasis ANDA applicants and created the potential for regulatory exclusivities that should not have existed.

200. First, all generic manufacturers that had submitted their ANDA applications *before* the second wave patents issued were required, as of the second wave patents' dates of issuance, to amend their ANDAs to include certifications with respect to each of those patents. Thus, after Allergan listed the second wave patents, the ANDA applicants were required to amend their ANDAs, either (1) by filing Paragraph III certifications to those patents (and thus waiting *many more years* for FDA approval) or (2) by filing Paragraph IV certifications to challenge those patents (thereby triggering Allergan's ability to bring immediate infringement litigation against them).

201. Second, by listing the second wave patents in the Orange Book, Allergan created

the space for it to argue, and the FDA to accept, that a 30-month stay of FDA approval for generic Restasis existed until at least 2018. Indeed, Allergan has taken this position in filings with the FDA and in filings with the *Allergan* court.

202. Third, by listing the second wave patents in the Orange Book, Allergan created the potential for one or more ANDA filers to argue that their Paragraph IV certification(s) to one or more of the second wave patents created a first-to-file exclusivity under which no other ANDA applicant could gain FDA approval for generic Restasis until 180 days after the first-to-file applicant entered the market. (At least two ANDA applicants, and Allergan itself, would later make this argument to the FDA).

203. Fourth, by obtaining the second wave patents, Allergan also created the potential for one or more ANDA filers to provide a Paragraph IV certification to a patent listed in the Orange Book prior to any second wave patents' issuance. That ANDA filer could then argue that its Paragraph IV certification to the prior-listed patent created a first-to-file exclusivity with priority over any first-to-file exclusivity flowing from a Paragraph IV certification of the second wave patents. Indeed, at least one ANDA applicant would later make this argument to the FDA.

204. Allergan knew when it listed the second wave patents in the Orange Book that those listings would impose unwarranted regulatory hurdles to ANDA approval, would likely allow Allergan to bring immediate suit against ANDA applicants, and would create the potential for unwarranted 180-day exclusivities. The purpose and effect of Allergan's second wave patent listings was to hinder and impede competition in the market for cyclosporine ophthalmic emulsion, 0.05%.

D. 2011 to 2014: About five manufacturers submitted generic Restasis ANDAs to the FDA.

205. Beginning in 2011, generic pharmaceutical manufacturers – including some of

the biggest brand and generic pharmaceutical companies in the world – submitted ANDAs seeking FDA approval to market cyclosporine ophthalmic emulsion, 0.05%.

206. The manufacturers *known* to have filed ANDAs by early 2014 are listed below.

ANDA Applicant	ANDA Number	Date of ANDA Submission (if known)[113]
Watson Pharmaceuticals, Inc.	203463	November 14, 2011
Teva Pharmaceuticals (now Actavis)	203880	Probably 2011, because of the first three digits (203)
Akorn Pharmaceuticals	204561	2012
Mylan Pharmaceuticals, Inc.	205894	None available.
InnoPharma, Inc.	206835	January 13, 2014

207. By the summer of 2015, the FDA had concluded that several of those ANDAs were substantially complete at the time they were first filed, many years earlier.

208. On July 28, 2015, the FDA issued a "Dear Applicant" letter, asking generic Restasis applicants to comment on issues concerning a 180-day exclusivity period for the first-filer of a Paragraph IV certification with respect to Restasis (i.e., whether any of the generic Restasis ANDA filers claimed this period of exclusivity for their generic Restasis product).[114]

209. Generic Restasis ANDA filers submitted responses to this FDA request, and these responses not only acknowledged generic Restasis ANDA filings, but also revealed their timing.

210. For example, the generic manufacturer InnoPharma, Inc. (a Pfizer subsidiary) has

[113] Discovery will show the actual ANDA submission dates.

[114] Letter from T. Jetton to Cyclosporine Ophthalmic Emulsion ANDA Applicants, Docket No. FDA-2015-N-2713-0001 (July 28, 2015).

revealed that in mid-2015, the FDA deemed its ANDA for cyclosporine ophthalmic emulsion, 0.05% to be substantially complete as of the ANDA's original filing date of January 13, 2014.[115]

211. To be deemed substantially complete, an ANDA must contain sufficient data to plausibly support an FDA determination that the applied-for generic product is bioequivalent to the corresponding brand product, including drug release-rate data. The FDA's determination that InnoPharma's ANDA was substantially complete when filed on January 13, 2014 means that the FDA could have made an approval determination on that date.

212. Another example comes from the generic manufacturer, Akorn Pharmaceuticals. Akorn appears to have filed an ANDA in 2012 that the FDA subsequently determined (in mid-2015) to have been substantially complete at the time it was filed. Akorn has revealed that the FDA acknowledged its ANDA on June 30, 2015, and the acknowledgment appears to relate back to Akorn's original ANDA filing in 2012.[116] During a March 22, 2016 earnings call, Akorn CEO Raj Rai indicated that Akorn had submitted its ANDA for Restasis in 2012.[117]

213. In public correspondence with FDA, Apotex (another ANDA filer) stated that it interpreted the FDA's "Dear Applicant" letter to all cyclosporine ophthalmic emulsion, 0.05% ANDA filers to necessarily imply that, by January 14, 2014, one or more ANDAs for that drug had been submitted and deemed substantially complete.[118]

---

[115] Letter from InnoPharma Licensing LLC to the Food & Drug Admin. at 3, Docket No. FDA-2015-N-2713-0002 (Aug. 26, 2015).

[116] Letter from Akorn Pharmaceuticals to the Food & Drug Admin. at 2, Docket No. FDA-2015-N-2713-0026 (Sept. 28, 2015).

[117] Transcript of Akorn's (AKRX) CEO Raj Rai on Business Update and 2016 Guidance Conference Call.

[118] Letter from Apotex Inc. to the Food & Drug Admin. at 8, Docket No. FDA-2015-N-2713-0003 (Aug. 26, 2015).

214. Allergan itself has stated, in its public correspondence with FDA, that it "understands" that "on or about July 9, 2015, FDA purportedly 'received' at least five ANDAs for review."[119] In that same public correspondence with FDA, Allergan stated that one of the ANDAs was submitted to FDA in 2013 and another was submitted as early as March of 2012.[120] Therefore, even Allergan agrees, given the FDA's definition for ANDA substantial completeness, that several ANDA filers had sufficient data to plausibly support FDA approval, including on the criterion of bioequivalence, as early as 2014.

E. 2014: Allergan begins a series of sham citizen petitions to the FDA.

1. January 2014: Allergan files its first sham citizen petition.

215. Another prong of Allergan's multi-faceted scheme was to delay the FDA's approval of any Restasis ANDA by filing repetitive, sham petitions to the FDA. With Ding I set to expire in May 2014, Allergan began to file, in January 2014, what would become a series of petitions attacking the FDA's articulated scientific basis for approving generic Restasis ANDA applications.

216. Allergan knew that its comments to the draft guidance would not necessarily delay generic entry: the FDA is only required to *consider* these comments it; is not required – as it is with a citizen petition – to *respond* to individual requests to take (or refrain from taking) action.

217. Therefore, starting in January 2014, despite having already aired its criticism of the FDA's draft guidance during the August 2013 comment period, Allergan began inundating

[119] Letter from Allergan, Inc. to the Food & Drug Admin. at 3, Docket No. FDA-2015-N-2713-0030 (Sept. 28, 2015).

[120] *Id.*

the FDA with submission after submission challenging the FDA's approach to determining the requirements for approving applications for generic cyclosporine ophthalmic emulsion products.[121]

218. Allergan claims that it submitted these citizen petitions to tell the FDA that "rushing prematurely to approve a proposed generic drug [not supported by in vivo clinical endpoint studies] poses a risk to patient health."[122] But Allergan's true goal was to delay the FDA's review of any Restasis ANDA. Allergan told investors that this tactic – saddling the agency with baseless, duplicative citizen petitions relating to the 2013 draft guidance – exemplified its response to "intense competition from generic drug manufacturers."[123]

219. On January 15, 2014, Allergan filed the first petition.

2. February 2014: Allergan amends its sham citizen petition.

220. On February 28, 2014, it filed another petition (the "February 2014 petition"), repeating the demands and arguments of the earlier one. This petition further added a required certification that acknowledged Allergan was aware of the existence of at least one specific instance of a generic company seeking to gain approval for a cyclosporine ophthalmic emulsion, 0.05% product. (Allergan later withdrew the earlier January petition, effectively allowing the

---

[121] *See* Letter from Allergan, Inc. to the Food & Drug Admin., Docket No. FDA-2014-P-0117 (Jan. 15, 2014) ("January 2014 Citizen Petition"); Letter from Damon Burrows, Vice President, Associate General Counsel, Allergan, Inc. to the Food & Drug Admin., Docket No. FDA-2014-P-0304 (Feb. 28, 2014) ("February 2014 Citizen Petition"); Letter from Dwight O. Moxie, Senior Attorney, Allergan Inc. to the Food & Drug Admin., Docket No. FDA-2015-P-0065 (Dec. 23, 2014) ("December 2014 Citizen Petition"); Letter from Thomas F. Poche, V.P. & Assist. General Counsel, Allergan, Inc. to the Food & Drug Admin. Docket No. FDA-2017-P-4745 (Aug. 4, 2017) ("August 2017 Citizen Petition").

[122] February 2014 Citizen Petition at 2.

[123] Allergan, Inc., Annual Report 12 (Form 10-K) (Feb. 18, 2015); *id.* at 48.

February petition to replace it.)

221. The February 2014 petition largely parroted Allergan's August 2013 comments to the FDA's June 2013 guidance. The petition challenged the FDA's decision to allow generic manufactures to use in vitro studies to establish bioequivalence for cyclosporine emulsion ophthalmic drug products. It made six demands of the FDA, including that it "withdraw the Draft Cyclosporine . . . and make clear that, bioequivalence for a proposed generic drug referring to RESTASIS can be demonstrated only through comparative clinical studies with appropriate clinical endpoints"[124]; that it "not accept for filing, but instead reject as incomplete, any ANDA referencing Restasis that does not include data derived from at least one comparative clinical endpoint study"[125]; and that it "make clear that it will not approve any ANDA referencing Restasis based exclusively on in vitro assays unless and until clinical studies have been performed sufficiently to validate that those in vitro assays correlate to relevant in vivo bioavailability in humans."[126]

222. The February 2014 petition cited to the public comments Allergan's cadre of paid doctors submitted, ostensibly "draw[ing] from their clinical experience, criticizing the draft guidance's in vitro approach."[127]

223. Allergan ostensibly supplemented the petition on May 29, 2014 and then re-submitted it on October 31, 2014.

3. November 2014: The FDA rejects Allergan's first sham petition.

224. On November 20, 2014, only months after Allergan filed the February 2014

[124] February 2014 Citizen Petition at 6.

[125] *Id.*

[126] *Id.*

[127] *Id.* at 4.

petition and only weeks after its re-submission, the FDA denied all of Allergan's substantive demands.

225. The FDA provided a thorough explanation of the scientific determination on which its draft guidance was based.

226. *The scientific rationale for the in vitro testing option*. The purpose of a bioequivalence study is to determine whether any formulation differences between a proposed generic product and the reference listed drug cause the active ingredient to reach the site of action at a different rate or to a different extent. There are two key concerns when determining bioequivalence of a locally acting topical ophthalmic product: (1) Are the test and reference products formulated similarly such that the release characteristics are the same between the two products?, and (2) Will the ocular tissues uptake the same amount of the drug, or will differences in formulation and/or manufacturing of the two products affect absorption?

227. The FDA considers comparative clinical endpoint studies to be relatively insensitive at detecting the manufacturing and formulation variables, which have the greatest potential to affect the bioavailability of topical ophthalmic products.[128] In particular, in vivo clinical endpoint studies (studies in live subjects), which measure formulation differences indirectly rather than directly, may be limited by confounding variables such as differing severities of the disease and differences in the definition of the instrument used to measure efficacy, among other issues.

228. As a result, in recent years, the FDA researched alternative, in vitro

[128] 21 C.F.R. § 320.24(b)(4) (stating that comparative clinical endpoint trials are "the least accurate, sensitive, and reproducible of the general approaches for measuring bioavailability or demonstrating bioequivalence").

bioequivalence testing methods that can be expected to detect meaningful differences in safety and therapeutic effect between generic and listed versions of non-systemically absorbed drugs (in vitro studies are studies conducted on blood, cells, or tissues in the laboratory setting).[129] The FDA has explored many different approaches to demonstrating bioequivalence for locally acting, non-systemically absorbed topical drug products, including approaches were the proposed generic products is both quantitatively and qualitatively the same as the reference listed drug.

229. When a generic product is quantitatively and qualitatively the same as the reference listed drug, the *only* differences it could have from the reference listed drug would be in its physicochemical properties. Such differences can arise only from differences in the generic product's manufacturing process and formulation steps, and they can affect the generic product's drug release, absorption, and dose uniformity. When a generic product's physicochemical properties and drug release rate are similar to those of the reference listed drug, bioavailability is expected to be the same for both products.

230. In recent years, based upon its research findings and other available information, the FDA has recommended in vitro studies for demonstrating the bioequivalence of several locally acting products when the formulations of the products are the same, including for cyclosporine ophthalmic emulsion, 0.05%.[130] As such, the 2013 draft cyclosporine guidance includes a recommended in vitro option for proposed product formulations that are quantitatively and qualitatively the same as the reference listed drug and that also meet other specified criteria.

---

[129] *See* 21 U.S.C. § 355(j)(8)(C).

[130] Prior to its recommendations on cyclosporine ophthalmic emulsion, 0.05%, the FDA had recommended in vitro testing for other drug products. For example, the FDA recommended that generic applicants demonstrate bioequivalence via in vitro methods for the following drug products with formulations that were quantitatively and qualitatively the same as their reference listed drugs: vancomycin capsules, acyclovir ointment (topical dermatological product), and budesonide inhalation suspension (an inhalation suspension).

231. In considering the most accurate, sensitive, and reproducible methodology to demonstrate bioequivalence, the FDA has also reviewed the option of conducting a comparative clinical endpoint study to demonstrate bioequivalence of cyclosporine ophthalmic emulsions. It concluded that a comparative clinical endpoint study likely *would not be as reliable* at detecting differences in the formulation and manufacturing process of a proposed generic product when the reference listed drug shows only a modest clinical effect.

232. The FDA also concluded that such trials might present economic and logistical challenges for ANDA sponsors. Nevertheless, the 2013 draft cyclosporine guidance provides an in vivo clinical endpoint option, and it recommends that a sponsor proposing to conduct such a trial first consult with the FDA by submitting the study protocol.

233. Based on these considerations, the FDA determined that, for cyclosporine ophthalmic emulsions, in vitro studies are likely more sensitive, accurate, and reproducible than comparative clinical endpoint studies. This determination is why the FDA's 2013 draft guidance includes an in vitro testing-only option.

234. *Comparing formulations that are quantitatively and qualitatively the same.* The FDA's recommended in vitro option for cyclosporine ophthalmic emulsion first provides that the proposed generic product formulation must be quantitatively and qualitatively the same as the reference listed drug (i.e., Restasis) because formulation differences (such as differences in the inactive ingredients) may alter cyclosporine bioavailability. The in vitro option is available *only* when it is confirmed that the identity and amount of each component in the proposed generic drug product is the same as that contained in the reference listed drug. For a proposed generic product that is not quantitatively and qualitatively the same as the reference listed drug, the in vivo study with a clinical endpoint would be the recommended option.

235. *Acceptable comparative physiochemical characterizations (Q3).* Of course, the FDA recognizes that even a generic product that is quantitatively and qualitatively the same as the reference listed drug can have clinically significant differences in its physiochemical profile owing to differences in the generic product's manufacturing and formulation processes. Accordingly, the FDA's 2013 draft guidance also recommends that an ANDA applicant seeking to establish bioequivalence solely through in vitro studies demonstrate that the proposed generic product has a physiochemical profile similar to that of the reference listed drug. It recommends that applicants perform comparative physiochemical characterization of globule size distribution, viscosity, pH, zeta potential, osmolality, and surface tension.

236. *Acceptable comparative in vitro release rates*. Finally, the FDA's in vitro option recommends that an ANDA applicant confirm that the cyclosporine release rate of its proposed generic product is comparable to that of the reference listed drug. An in vitro release rate reflects the combined effect of several physical and chemical properties in both the drug substance and the drug product. Manufacturing methods and processes (e.g., heating, mixing, or cooling) may change the formulation's attributes, thereby affecting the rate of drug release and the drug's bioavailability. Confirmation that a proposed generic product has a comparable release rate to that of the reference listed drug can help ensure that the proposed generic product will deliver cyclosporine to the ocular tissues for absorption in a manner comparable to that of the reference listed drug.

237. In sum, the FDA has determined that a proposed cyclosporine ophthalmic emulsion formulation that meets the three recommended criteria – quantitative and qualitative sameness, physiochemical sameness, and an acceptable comparative in vitro release rate – should become available at the site of action at a rate and to an extent that is not significantly different

than that of the reference listed drug. Thus, a proposed generic product that meets these three requirements has sufficiently demonstrated bioequivalence. Whether the data and information in a particular ANDA are sufficient to demonstrate bioequivalence is an issue the FDA determines during review of the specific ANDA.

238. The FDA rejected each of the scientific and legal positions Allergan asserted in its February 2014 petition.

239. With respect to the science, the FDA noted the exacting requirements of its in vitro option (as set forth in the 2013 draft guidance); namely, that an "in vitro option is available *only* when it is confirmed that the identity and amount of each component in the proposed generic drug product is the same as that contained in the [reference listed drug]. For a proposed generic product that is not [quantitatively and qualitatively] the same as the [reference listed drug], the in vivo study with a clinical endpoint would be the recommended option."[131] Recognizing that even those products that are quantitatively and qualitatively the same can, through formulation or manufacturing differences, have different bioavailability, the in vitro option also requires an ANDA applicant to "demonstrate that the proposed generic product has a physiochemical profile acceptably similar to that of the [reference listed drug] . . . [by] perform[ing] . . . comparative physiochemical characterization to assure that . . . generic formulations can be expected to deliver the same amount of drug for absorption at the site of application as the [reference listed drug]," through measuring the seven characteristics of "globule size distribution, viscosity, pH, zeta potential, osmolality, and surface tension."[132]

[131] Letter from the Food & Drug Admin. to Allergan, Inc. at 13, Docket No. FDA-2014-P-0304-0042 (Nov. 20, 2014) ("FDA Nov. 2014 Response to Allergan Feb. 2014 Citizen Petition").

[132] *Id.* at 14.

240. The FDA observed that it was "confident" the in vitro option had "general scientific validity" under any reasonable standard of that concept. Its guidance was "substantiated by scientific evidence," including peer-reviewed research conducted by the FDA's Office of Testing and Research.[133] Allergan's criticisms of the FDA's research "were simply outside the scope" of the FDA's publication.[134] The FDA observed that Allergan "offer[ed] no evidence" to support its position that the FDA's proposed measurements of certain physiochemical properties were insufficient to measure bioavailability on the basis of current science.[135] The FDA also rejected Allergan's claim that current methods of testing were inadequate. It rejected Allergan's claim that the testing methods inadequately assessed safety and efficacy, concluding there was "no merit to this argument."[136] It rejected Allegan's attempt to use the FDA's prior rejection of in vitro data in a completely separate context to undermine the FDA's conditional acceptance of in vitro data to prove the bioequivalence of cyclosporine ophthalmic emulsion, 0.05% products. And it rejected Allergan's attack on FDA's release-rate testing requirement, noting that the guidance recommends that "'[a]cceptable comparative in vitro drug release rate tests' be performed on the reference listed drug and test formulation, and the burden is on ANDA applicants to develop a suitable in vitro method for measuring drug release, not on FDA to prescribe one."[137]

241. Finally, the FDA noted that the alternative to in vitro testing – in vivo testing – was inferior. It stated:

---

[133] *Id.* at 16-17.

[134] *Id.* at 17 n.55.

[135] *Id.* at 18.

[136] *Id.* at 20.

[137] *Id.* at 25.

> Because comparative clinical endpoint studies measure formulation differences indirectly rather than directly, it is more likely that in vivo testing will result in erroneous determinations of bioequivalence than in vitro testing. Thus, we believe that the most accurate, sensitive, and reproducible methodology to demonstrate bioequivalence likely will be in vitro testing, as recommended in the Draft Cyclosporine BE Guidance. Moreover, given the modest clinical benefit shown for cyclosporine ophthalmic emulsion, such a comparative clinical endpoint study could require more than 2,000 subjects with dry eye disease to pass the statistical tests for bioequivalence. Consequently, we recognize that a comparative clinical endpoint study may pose economic and logistical feasibility concerns.[138]

242. As to Allergan's arguments on the law, the FDA concluded that "[n]one of your legal conclusions has merit."[139]

243. The FDA summed up its rejection of Allergan's complaints, stating that the in vitro-only option in its June 2013 draft guidance was consistent with "the Agency's authority to make bioequivalence determinations on a case-by-case basis using in vivo, in vitro, or both types of data."[140] This authority enabled the FDA "to effectuate several long-standing policies that protect the public health" when approving ANDAs for generic drugs.[141] Those policies included "(1) refraining from unnecessary human research when other methods of demonstrating bioequivalence meet the statutory and regulatory standards for approval; (2) permitting the Agency to use the latest scientific advances in approving drug products; (3) protecting the public by ensuring only safe effective generic drugs are approved for marketing; and (4) making more safe and effective generic drugs available."[142]

---

[138] *Id.* at 26 (footnotes omitted).

[139] *Id.* at 27.

[140] *Id.* at 7.

[141] *Id.*

[142] *Id.* at 7-8 (footnotes omitted).

244. The FDA rejected each and every factual and legal argument as well as every substantive demand Allergan posited in its February 2014 petition. The only demands that it "allowed" (in quotations given the pyrrhic nature of the grant) were (1) an opportunity to comment on the guidance (which, of course, Allergan had already been given), and (2) an articulation of the basis for FDA's guidance decision (which it had already done, and was required to do in response to any petition on the subject, regardless how frivolous the demand might be).

245. After the FDA issued its November 20, 2014 rejection of Allergan's petition, Allergan did not appeal that decision. An appeal of that decision in the courts might eventually resolve the issues (likely against Allergan), but that would not hinder the FDA's ordinary course review of then-pending ANDAs for generic Restasis products.

4. December 2014: Allergan files yet another sham citizen petition.

246. On December 23, 2014 – only four weeks later – Allergan filed yet another petition with the FDA (the "December 2014 petition").

247. The December 2014 petition largely repeated the positions Allergan set forth in its February 2014 petition. The December 2014 petition again demanded that the FDA require Restasis ANDA filers to conduct in vivo testing only.

248. Allergan supplemented the December 2014 petition four times, including an August 16, 2015 supplement in which Allergan demanded (among other things) that the FDA convene a committee of outside experts to evaluate the use of in vitro methods for testing generic Restasis. Allergan further demanded that the FDA refuse to receive, review, or approve any generic Restasis ANDAs until that outside committee's evaluation was complete.

249. At the time Allergan filed the December 2014 petition, no reasonable company would have a realistic expectation that the FDA would adopt any of the substantive demands

made in the petition. The FDA had already addressed and rejected most of the arguments Allergan made in the December 2014 petition. That petition, and its supplements, provided no new, reliable, clinically relevant information upon which the FDA could allow, consistent with its statutory mandate to make decisions based on science and the law, Alleran's regulatory positions.

5. February 2016: The FDA rejects Allergan's second petition.

250. On February 10, 2016, the FDA denied all of the substantive demands made by Allergan in its December 2014 petition and various supplements to it (the "February 2016 rejection"). In doing so, the FDA rejected each of the scientific and legal positions Allergan took in its petition.

251. The FDA first noted that the December 2014 petition "repeats many of the assertions that were at the center of Allergan's previous petition."[143] Those assertions, the FDA found, were largely not worth further response from the agency.

252. The FDA also observed that many of Allergan's complaints treated the draft guidance in a conceptually inaccurate way; Allergan was treating a draft guidance as a final, immovable position. But as the FDA pointed out, the document clearly "informs the reader via a conspicuously placed text box that the 'draft guidance, *once finalized*, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.'"[144] Since the draft guidance "is a living, science-based document that is subject to change as new data and information on cyclosporine ophthalmic emulsion become available,"[145] Allergan's treatment of it as a static

[143] Letter of Food & Drug Admin. to Allergan, Inc. at 13, Docket No. FDA 2015-P-0065-0027 (Feb. 10, 2016) ("FDA Feb. 2016 Response to Allergan Dec. 2014 Citizen Petition").

[144] *Id.* (emphasis in original).

[145] *Id.* at 14.

position was incorrect. (Indeed, on the same day that the FDA denied the petition, the FDA issued modifications to the in vitro recommendations in the draft guidance to refine several requirements in the physiochemical characterization and statistical analysis).

253. The FDA rejected, once again, Allergan's rehashed arguments about the ostensible need to show an established in vitro-in vivo correlation (IVIVC). And the FDA rejected Allegan's citation to FDA-funded research on topical ophthalmic suspensions and emulsions as having "no bearing on the scientific validity" of the draft guidance.[146] Among other reasons, that research did not even involve cyclosporine ophthalmic emulsion. It rejected Allergan's citation to a statement attributed to a United States Pharmacopeia Expert Panel; since that panel "did not support [the] statement with evidence,"[147] there was no reason for FDA to credit it.

254. The FDA also rejected Allergan's assertion that in vitro testing of physiochemical properties of emulsions that are quantitatively and qualitatively the same is invalid for determining bioequivalence. It found "misleading" Allergan's characterizations of comments made at an April 2015 public meeting. Because Allergan had repeated arguments about its NDA emulsion tests, the FDA reexamined that data: the FDA wrote it "still find[s] that none of Allergan's test emulsions [were] comparable to Restasis" such that arguments about their lack of bioequivalence were unhelpful.[148] And Allergan had not even *tried* to determine if those emulsion examples had comparative release rates. As the FDA put it, Allergan "did not follow" the draft guidance it attacked. As the FDA explained, Allergan's claim that the in vitro testing

[146] *Id.* at 18.

[147] *Id.* at 19.

[148] *Id.* at 24-25.

was invalid "confuses a scientific obstacle (which FDA expects applicants to overcome to support approval) for a scientific impossibility."[149]

255. The FDA's February 2016 rejection details other flaws of Allergan petition. The FDA was "unable to respond" to Allergan's assertion that the FDA had not acknowledged "other directly relevant data" because "Allergan did not specify the other data that it contends we ignored."[150] Allergan's presentation of globule size distributions used neither instrumentation nor a methodology "appropriate for the pivotal comparisons" envisioned by the guidance.[151] Indeed, Allegan did not even use the same methodology to measure the test batches than that it used to measure the reference product – a fatal, scientific flaw. Allergan's citation to the FDA's recommendations for in vivo-only bioequivalence testing for solution or suspension products had no relevance to cyclosporine emulsion; the FDA's "bioequivalence recommendations are determined on a case-by-case basis depending on the drug under study,"[152] not for groups of different products with different characteristics. Allergan also "exaggerate[d]" the significance of the FDA's extensive comments for in vivo testing of other topical ophthalmic products. As the FDA put it, "the degree of thought that FDA put into developing these guidances cannot be divined"[153] from the number of comments the FDA provides.

256. The FDA concluded it "has clear legal authority to receive and approve an ANDA for cyclosporine ophthalmic emulsion that relies exclusively on in vitro testing data."[154] As a

[149] *Id.* at 30.

[150] *Id.* at 31.

[151] *Id.* at 33.

[152] *Id.* at 36.

[153] *Id.* at 37.

[154] *Id.* at 44.

result, the FDA, once again, rejected all of Allergan's substantive demands. The FDA did agree (1) to disclose (as it had already done) the in vitro bioequivalence methods it intended to accept for ANDAs that refer to Restasis, and (2) to respond specifically to the Allergan's testing of nine experimental test emulsions (and, in doing so, rejected them as scientifically unreliable).

257. After the FDA issued its February 2016 rejection of Allergan's December 2014 petition, Allergan did not appeal that decision. Appealing the decision in the courts might eventually resolve the issues (likely against Allergan), but that would not hinder the FDA's ordinary course review of then-pending ANDAs for generic Restasis products.

258. In 2016, the FDA issued amendments to its draft guidance for cyclosporine ophthalmic emulsion products. Allergan commented on those revisions.

6. August 2017: Allergan files a third citizen petition to the FDA.

259. On August 4, 2017, Allergan filed yet another petition with the FDA (the "August 2017 petition"), once again attacking the FDA's articulated scientific basis for approving generic Restasis. This petition predictably requested – again – that the FDA refuse to accept or approve any pending ANDAs unless supported by in vivo clinical endpoint studies.[155] Allergan supplemented this petition on October 13, 2017.[156]

260. At the time that Allergan filed the August 2017 petition, no reasonable company would have a realistic expectation that the FDA would adopt any of the substantive demands made in the petition. The FDA had already addressed and rejected most of the arguments it made in this petition. The August 2017 petition, and its supplement, provided no new, reliable, clinically relevant information upon which the FDA could allow, consistent with its statutory

[155] August 2017 Citizen Petition at 1.

[156] Supplement to Allergan's August 4, 2017 Citizen Petition, Docket No. FDA-2017-P-4745 (Oct. 13, 2017) ("October 2017 Supplement").

mandate to make decisions based on science and the law, its regulatory positions.

F. June 2015: The FDA acknowledges added regulatory challenges arising from Allergan's January 2014 listing of the '111 patent in the Orange Book.

261. Up until January 2014, all of the ANDAs pending with the FDA (four in total) were filed with Paragraph III certifications of the Ding I patent. In other words, all of the manufacturers that filed ANDAs before January 2014 were prepared to wait until Ding I expired in May 2014 for FDA approval and launch. The first ANDA was filed in November 2011; two others were filed in 2012. Thus, by January 2014, three of the four ANDAs had been pending with the FDA for two or more years.

262. Allergan's procurement and listing of the first second wave patent in the Orange Book on January 14, 2014 created a series of consequences, all of which furthered Allergan's scheme.

263. First, as soon as the second wave patents began to issue, all of the then-pending ANDAs had to be amended to include either Paragraph III or Paragraph IV certifications with respect to the new second wave patents. A Paragraph III certification would have meant the ANDA holder was prepared to wait until the second wave patents expired for FDA approval and launch (*e.g.*, 2024). This prospect was highly unlikely. Paragraph IV certifications, on the other hand, attested to the invalidity or non-infringement of the newly listed patents and signaled to the FDA that the ANDA holder was looking to market its generic drug as soon as possible. All of the ANDAs that were pending with the FDA as of January 14, 2014 were amended to include Paragraph IV certifications to the newly listed second wave patents.

264. Second, these Paragraph IV certifications enabled Allergan to sue each ANDA holder for infringement of the newly listed second wave patents. Ordinarily, the timely filing of a patent infringement action upon receipt of a Paragraph IV certification triggers an automatic 30-

month stay of FDA approval. But because these Paragraph IV certifications came by way of amendments to already pending ANDAs, which the FDA later determined were substantially complete when filed, no 30-month stay technically applied to any of them.[157] Allergan, however, repeatedly disputed the non-existence of the 30-month stays as to all the ANDA holders. Allergan pressed that, as a result of the automatic, 30-month stays, the FDA could not approve *any* ANDA pending resolution of the patent infringement litigation.

265. Third, the Paragraph IV certifications also obligated the FDA to direct resources towards resolving whether one or more of the certifications created first-to-file exclusivity for a particular generic manufacturer. If such exclusivity existed, no other ANDA applicant could gain FDA approval for its generic Restasis until 180 days after the first-to-file applicant entered the market. Because the 180-day market exclusivity period in this case could amount to hundreds of millions of dollars in additional revenue to the first-filer, the Paragraph IV certifications altered the motives of each ANDA holder. Each had a compelling incentive to convince the FDA of its first-to-file status. Given these stakes, the FDA generally makes its first-to-file decisions very carefully so as to reasonably avoid lawsuits from disappointed ANDA filers. Accordingly, first-to-file decision-making – flowing from Allergan fraudulently obtaining the second wave patents and then improperly listing them in the Orange Book – has the capacity to slow the FDA ANDA approval process.

266. Fourth, Allergan's procurement of the second wave patents created the opportunity for one or more ANDA filers to provide a Paragraph IV certification as to the Ding I

[157] 21 U.S.C. § 355(j)(5)(B)(iii). The automatic, 30-month stay technically applied to the following Paragraph IV-certified ANDAs: Apotex, Famy Care, TWi, Deva, Saptalis, and Amneal. All of these ANDAs were filed with the FDA after Allergan's January 2014 Orange Book listing of the first second wave patent.

patent (the older, already-listed Orange Book patent). In so doing, the ANDA filer would present the FDA with a separate and competing track of first-to-file exclusivity determinations. Seizing the opportunity Allergan created, one generic filer, InnoPharma, did exactly that.

267. In early December 2013, the Official Gazette of the PTO publicly disclosed that the PTO would issue the first second wave patent on January 14, 2014. InnoPharma first filed its ANDA on January 13, 2014 – the day before the first second wave patent issued. InnoPharma's ANDA was the *first* and *only* ANDA to contain a Paragraph IV certification to the Ding I patent. Absent knowledge that the first second wave patent would issue, no reasonable ANDA applicant in InnoPharma's position would have expected the FDA to approve its ANDA within the four months before Ding I expired. InnoPharma, however, took advantage of the opportunity created by Allergan's scheme, likely filing its Paragraph IV to Ding I in the hopes of: obtaining a regulatory advantage with the FDA, securing a better negotiation position with Allergan for later settlement purposes, and/or negating any first-filer exclusivity that might otherwise be awarded to a competing generic manufacturer. In any event, InnoPharma's Paragraph IV certification to Ding I – a natural consequence of Allergan's fraudulent procurement of the first second wave patent – added material complexity to the challenging first-filer determination the FDA faced and only furthered any slowdown in the FDA's ANDA approval process.

268. In July 2015, the FDA acknowledged the difficulties it faced as a result of Allergan's January 2014 procurement and listing of the first second wave patent in the Orange Book. In a July 28, 2015 "Dear ANDA Applicant" letter, the FDA solicited the views of *all* the ANDA filers regarding which ANDA applicant should be deemed the first-filer. Allergan used the "Dear ANDA Applicant" letter as an opportunity to demand, again, as it had in its citizen petitions, that the FDA refuse to approve any ANDA that was not supported by clinical end-point

studies.[158] Allergan also advocated that the FDA find no forfeiture of the 180-day exclusivity had occurred (likely in an effort to keep the option of a no-authorized generic settlement available). In doing so, Allergan sought to further complicate the FDA's first-filer decision-making process and delay any FDA ANDA approvals. To this day, the FDA has not yet publicly made its first-filer determination.

269. The first-filer uncertainty created by Allergan's procurement and Orange Book listing of the second wave patents also led to Teva's October 17, 2018 filing of an action in the United States District Court for the District of Columbia. Through this action, Teva sought a court declaration and order barring the FDA from awarding first-filer status to any other ANDA applicant – again, the FDA had to direct resources to addressing the first-filer uncertainty created by Allergan's obtaining by fraud and improperly listing the Second Wave patent. In response to that action, the FDA argued that the reality that it has not yet approved an ANDA for Restasis, much less Teva's, required the Court to dismiss the action on ripeness grounds. To avoid further litigation on this issue, the FDA now has an incentive *not* to review and approve an ANDA while Teva's action remains pending. As of the filing of this complaint, Teva's action remains pending.

G. August 2015: Allergan begins a series of sham patent infringement lawsuits.

270. In the midst of filing these sham citizen petitions, Allergan also initiated sham lawsuits against its would-be generic competitors. In response to Allergan's Orange Book listings, exactly as Allergan had planned, generic competitors were forced to submitted original or amended Paragraph IV certifications to the FDA with respect to the second wave patents.

271. On or about June 2015, the FDA acknowledged receipt of several ANDAs for

[158] Ltr. from D. Moxie to Division of Dockets Management (HFA-305), FDA, Re: Docket No. FDA-2015-N-2713—Abbreviated New Drug Applications for Cyclosporine Ophthalmic Emulsion (Sept. 28, 2015).

cyclosporine ophthalmic emulsion, 0.05%. Upon the FDA's acknowledgement of these ANDAs, several generic manufacturers (Apotex, Akorn, Mylan, and Teva) served notices of their Paragraph IV certifications on Allergan starting in July 2015. The Paragraph IV notices asserted that the second wave patents either were invalid or non-infringed. Several other ANDA filers would later follow suit. The table below summarizes when generic manufacturers served their Paragraph IV notices on Allergan.

272. In August of 2015 – after receiving the Paragraph IV notices its Orange Book listings triggered – Allergan filed suit against Akorn, Teva, Apotex, and Mylan in the Eastern District of Texas. Allergan alleged infringement of various claims in the first five of the six second wave patents.

273. Over time and as additional generic makers served notice of their ANDAs and Paragraph IV certifications on Allergan, Allergan filed additional suits against its would-be competitors. The table below summarizes when Allergan filed these lawsuits.

Defendant	Paragraph IV Notice Received	Complaint Filed	Patents
Teva Pharmaceuticals	07/23/15	08/24/15	'111, '162, '556, '048, '930
Apotex	07/24/15	08/24/15	'111, '162, '556, '048, '930
Akorn Pharmaceuticals	07/13/15	08/24/15	'111, '162, '556, '048, '930
Mylan Pharmaceuticals, Inc.	07/21/15	08/24/15	'111, '162, '556, '048, '930
InnoPharma, Inc.	08/03/15	09/08/15	'111, '162, '556, '048, '930
Famy Care Ltd.	03/01/16	04/12/16	'111, '162, '556, '048, '930, '191
TWi Pharmaceuticals	06/09/16	07/20/16	'111, '162, '556, '048, '930, '191
Deva Holdings	11/11/16	12/22/16	'111, '162, '556, '048, '930, '191

Saptalis Pharmaceuticals, LLC	6/27/18	8/10/18	'162, '556
Amneal Pharmaceuticals LLC	8/9/18	9/19/18	'162, '556

274. No reasonable brand company would have a realistic expectation of prevailing on the merits of the second wave patent litigation.

275. Federal court patent litigation affords parties the opportunity to conduct orderly construction of the applicable patent claims, reveal the actual facts that lurk behind broad misstatements, compare the timing of claimed inventiveness to the true prior art publication dates, and determine the merits of validity and infringement of patents.

276. In the stark light of federal patent litigation, no reasonable litigant in Allergan's position would have realistically expected to avoid invalidation of the second wave patents. These patents were obviousness in light of the prior art as of their September 2003 priority date.

277. First, the second wave patents were *prima facie* obvious in light of the Ding I patent and the Sall and Stevenson publications. Allergan itself conceded this reality in unequivocal terms during its prosecution of the '857 patent.

278. Second, Allergan was cornered into taking the position that, as of the priority date of September 2003, it had uncovered some unexpected and surprising attributes of the 0.05% cyclosporine formulation as compared to the 0.1% formulation. But the data Allergan relied on to reach that conclusion dated back *to its own clinical trials in the 1990s* – the results of which were published *in 2000* in articles that served as prior art to the second wave patent applications.

279. Third, any reasonable litigant would not expect a federal court to accept the machinations to which Allergan's declarants were required to go, including: (1) rejecting the express conclusions of Allergan's prior publications, (2) deleting p-values and error bars in

figures submitted to the PTO to hide that comparisons of the 0.05% and 0.1% cyclosporine formulations were not statistically significant, (3) comparing results from disparate dry eye tests, (4) comparing the results from differing patient populations (i.e. comparing patient populations with varying severity of dry eye); (4) manipulating data through misleading ratio-of-ratios calculations, ignoring the vast majority of test results in favor of a few outlier outcomes; (5) relying on median changes from baseline rather than means; (5) and ignoring the critical fact the outcomes discussed were disclosed in prior art to the second wave applications; and (6) misconstrued basic pharmaceutical principles.

280. Fourth, the second wave patents had been procured by fraud. Allergan knew this. Its enforcement of them was a sham.

281. Finally, while not dispositive of the sham nature of the second wave litigation, the results of that litigation show the plausibility of the allegation that there was no realistic expectation of a win by Allergan on the ultimate merits.

H. December 2015: Allergan settles pending *inter partes* proceedings to forestall invalidation of the second wave patents.

282. Allergan's latest effort to forestall competition in the market for cyclosporine ophthalmic emulsion, 0.05% stems from a series of *inter partes* review requests.

283. In June 2015, Apotex petitioned the Patent Trial and Appeals Board (the "Board") to initiate an *inter partes* review of the second wave patents (Apotex subsequently provided notice of its Paragraph IV certifications to Allergan on July 23, 2015).

284. Allergan settled the Apotex *inter partes* proceedings in December 2015, on undisclosed terms, just days before the Board was set to rule on the likelihood that it would invalidate the second wave patents.

285. Allergan's settlement of Apotex's *inter partes* proceedings effectively forestalled – by at least a year – any risk that any one of the second wave patents would be invalidated by *inter partes* review proceedings.

I. September 2017: Allergan enters an anticompetitive agreement with the Saint Regis Mohawk Tribe to avoid invalidation of the second wave patents.

286. In June 2016, Mylan similarly petitioned the Board to initiate an *inter partes* review of the second wave patents. In December 2016, the Board resolved the same question that Allergan's settlement with Apotex mooted the year prior: The Board concluded there was a reasonable likelihood that each of the second wave patents would be invalidated upon the Board's further review. That conclusion triggered subsequent proceedings against all six second wave patents.[159]

287. Teva, Akorn, and Famy Care then filed their own *inter partes* review petitions. The Board joined these petitions with Mylan's *inter partes* proceeding.

288. On September 8, 2017, Allergan entered into an ostensible agreement with the Saint Regis Mohawk Tribe to convey ownership of the second wave patents to the tribe with an exclusive license back to Allergan for all FDA-approved uses in the United States. The agreement also included a promise from Mohawk that it would not waive its sovereign immunity with respect to any *inter partes* review or other administrative action in the PTO related to the second wave patents. The agreement further provided for a payment *to Mohawk* of $13.5 million

[159] Because the terms of Allergan's settlement with Apotex in December 2015 (that avoided the risk the second wave patents would be invalidated for as much as a year) were not made public, Plaintiffs are presently unable to determine the extent to which that settlement may have violated *FTC v. Actavis*, 570 U.S. 136 (2013), and thereby constitute another component in Allergan's overall scheme.

from Allergan, plus potentially $15 million in annual royalties.[160]

289. On the same day that Mohawk and Allergan entered into their purported transfer of property rights – less than a week before the scheduled *inter partes* hearing – Mohawk petitioned the Board to dismiss the pending *inter partes* reviews for lack of jurisdiction based on tribal sovereign immunity.[161]

290. No objectively reasonable litigant could expect these obstructionist tactics to succeed. Courts have rejected similar schemes to game the law, including in the context of sovereign tribes where the only interest the tribe had was in being paid for the cover of immunity.[162]

291. The *Allergan* court allowed Mohawk to be joined as a co-plaintiff, but only to ensure that any judgment it rendered would apply to Mohawk. The Court explained that despite its "serious concerns about the legitimacy of the tactic that Allergan and the Tribe have employed,"[163] it would "adopt the safer course of joining the Tribe as a co-plaintiff, while leaving the question of the validity of the assignment to be decided in the [*inter partes* review] proceedings."[164]

292. Allergan has made no secret of its subjective bad faith in adding Mohawk as a defendant in the *inter partes* reviews. Allergan's chief executive, Brent Saunders, explicitly

---

[160] *See* Brenda Sandburg, *Allergan May Rue Mohawk Tribe Deal as Court Invalidates Restasis Patents*, Pink Sheet (Oct. 16, 2017), https://pink.pharmaintelligence.informa.com/PS121779/Allergan-May-Rue-Mohawk-Tribe-Deal-As-Court-Invalidates-Restasis-Patents.

[161] Decision at 1, *Mylan Pharmaceuticals Inc. v. Saint Regis Mohawk Tribe*, Case IPR2016-01127 (PTAB Feb. 23, 2018) (Paper No. 132).

[162] *See, e.g.*, *People ex rel. Owen v. Miami Nation Enter.*, 386 P.3d 357 (Cal. 2016).

[163] Tribe Joinder Op. at 4.

[164] *Id.* at 9.

acknowledged that Allergan pursued the deal with Mohawk not to advance competition on the merits, but rather to avoid "double jeopardy" – that is, to intentionally disrupt one of the two adjudicative proceedings (the federal district court proceedings or the *inter partes* review proceedings). However, this stated rational ignores the fact that Allergan itself initiated the federal district court proceedings and could voluntarily dismiss them at any time.

293. Mohawk, for its part, entered the agreement for the money. Mohawk is not entering the pharmaceutical industry. In fact, Mohawk has publicly disclaimed any actual business interest in the pharmaceutical industry.[165] Licensing the second wave patents back to Allergan was not a natural outgrowth of any ownership interest Mohawk had prior to September 2017. And, from Mohawk's comments, the agreement was not made pursuant to a natural future interest either. In entering this contract, Mohawk was not acting in its sovereign capacity (e.g., regulating the sale or use of cyclosporine ophthalmic emulsion, 0.05% on a reservation) and was obtained no value for the ownership of the patents. While the license agreement excluded pharmaceutical use by Mohawk and permitted all other uses, Mohawk cannot exploit the inventions outside of the pharmaceutical realm because the patents are limited to pharmaceutical use.

294. In February 2018, the Board denied Mohawk's motion. It determined that Mohawk's "assertion of its tribal immunity does not serve as a basis to terminate these proceedings" and that Allergan retained "'all substantial rights' in the challenged patents."[166]

---

[165] *See* Saint Regis Mohawk Tribe Office of Technology, Frequently Asked Questions About New Research and Technology (Patent) Business at 1, https://www.srmt-nsn.gov/_uploads/site_files/Office-of-Technology-Research-and-Patents-FAQ.pdf ("[T]he Tribe is not investing any money in this business. Its only role is to hold the patents, get assignments, and make sure that the patent status with the US Patent Office is kept up to date.").

[166] Decision at 18, 20, *Mylan Pharmaceuticals Inc. v. Saint Regis Mohawk Tribe*, Case IPR2016-01127 (PTAB Feb. 23, 2018) (Paper No. 132).

Allergan and Mohawk filed a joint notice of appeal from that decision.

295. In that appeal, the United States Department of Justice filed a brief in support of affirmance, stating that the "evident purpose of" Allergan and Mohawk's deal "was to allow Allergan to retain and enforce its patents without risk of an adverse decision in the inter partes review." "In effect, the commercial rental of a tribe's sovereign immunity to a pharmaceutical company."[167]

296. In July 2018, the Federal Circuit affirmed. In November 2018, the Federal Circuit issued its mandate to the Board after denying Allergan's petitions for rehearing, *en banc* review, and a stay pending certiorari. On January 7, 2019, the Board advised that it would rely on the existing record to issue a final decision on the patent merits in due course.

J. October 2017: A federal district court invalidates the second wave patents after trial.

297. In its litigation against the generics, Allergan originally asserted all six of its patents against the generics (for a total of 157 patent claims). Because these 157 claims substantially overlapped with one another, Allergan ultimately reduced its asserted claims to thirteen unique claims to be resolved at trial. Allergan agreed that the outcome of this trial would govern *all* claims Allergan had previously asserted against the generics across all six patents. In connection with this claim reduction process, Allergan agreed to drop the '162 and '556 patents as duplicative of the thirteen claims arising from the other four second wave patents to be tried.

298. The generic manufacturers raised concern that by merely dropping the '162 and '556 patents, Allergan left open the possibility that it could raise each or both of these patents in subsequent proceedings (*i.e.*, if Allergan received an adverse judgment at trial on the four other

[167] *Brief for the United States as Amicus Curiae in Support of Appellees* at 2, No. 2018-1638 (Fed. Cir. filed May 11, 2018).

second wave patents). During the August 1, 2017 pretrial conference, the Court made clear that the objective was "to make sure that this matter is dispositive of the entire dispute between the parties." The Court clarified that, for purposes of the Hatch-Waxman proceedings, the trial on the thirteen representative claims would "dispose of all the disputes." The Court wanted to be sure that, later on, there would be no additional claims or infringement arguments. Allergan's counsel agreed: "any remedy that your Honor might enter as to the representative claims would apply equally to the unasserted claims."[168]

299. When Allergan appeared to balk at providing the generic manufacturers with covenants not to sue based on the dropped '162 and '556 patents, the matter was raised to the Court again in the August 27, 2017 final, pre-trial conference. In response, the Court reiterated that "it was pretty clear what the intent was, which was to have this entire dispute turn on the resolution of these 13 claims that are in suit, and that there wouldn't be anything left over either way." Upon learning that the parties were in agreement conceptually, the Court advised that "it should not be hard to cobble together language that will solve the problem." If there were issues drafting that language, the Court noted that it would make itself available to fully resolve the matter.[169]

300. Trial commenced the following day. Following the conclusion of that trial, on October 16, 2017, the Eastern District of Texas held the second wave patents were invalid for obviousness. Judge William C. Bryson of the United States Court of Appeals for the Federal Circuit presided over this trial, sitting on the Eastern District of Texas by designation. In an

[168] Aug. 1, 2017 Conf. Trans. at 7-8, *Allergan, Inc. v. Teva Pharmaceuticals USA, Inc.*, 15-cv-01455 (E.D. Tex.).

[169] Aug. 23, 2017 Conf. Trans. At 73-74, *Allergan, Inc. v. Teva Pharmaceuticals USA, Inc.*, 15-cv-01455 (E.D. Tex.).

extremely thorough opinion, the *Allergan* court found that Allergan had secured the second wave patents by "paint[ing] a false picture" of the relevant data.[170] As the Court explained, Allergan had conceded in 2009 that the Restasis formulation would have been "readily envisage[d]" from the Ding I patent.[171] And the data Allergan relied on to show unexpected results did not, in reality, demonstrate anything unexpected. In any event, this data was actually prior art and could not be relied on to prove the patentability of the second wave patents.

301. Despite this litigation's lack of objective merit, Allergan pressed its claims for years.

302. The objective merits were irrelevant, however, to Allergan's true purpose. Allergan filed suit not to vindicate any legitimate patent infringement issues, but to frustrate the introduction of generic Restasis products on the market. Its motives were financial: every extra month Allergan could delay competition on Restasis added another $125 million to its revenues.

303. In November 2018, after Allergan's appeal of the trial judgment was exhaustively briefed and argued, the Federal Circuit issued a one-word decision: "AFFIRMED."[172]

K. January 2018: The FDA rejects Allergan's third citizen petition.

304. On January 2, 2018, the FDA rejected Allergan's third petition in its entirety.

305. Given the repetitive and unsupported nature of the issues this petition once again posited, the FDA's rejection was brief. And once again, it reminded Allergan of the publicly stated requirements for approval of generic Restasis.

306. The FDA has not made any of the changes Allergan requested in its third citizen

[170] *Allergan*, 2017 WL 4803941, at *39.

[171] *Id.* at *9.

[172] *Allergan, Inc. v. Teva Pharmaceuticals USA, Inc.*, 742 Fed. Appx. 511 (Fed. Cir. 2018).

petition to the Draft Guidance on Cyclosporine. The FDA has not made any changes to the Draft Guidance since October 2016.

L. August to September 2018: Allergan files two new sham patent infringement suits against Saptalis and Amneal.

307. Upon receipt of Paragraph IV notifications from Saptalis Pharmaceuticals, LLC and Amneal Pharmaceuticals LLC in 2018, Allergan, joined by its co-conspirator, Mohawk, instituted patent infringement actions in the United States District Court for the District of Delaware. In both actions, Allergan and Mohawk were jointly represented by the *same* attorneys who represented Allergan in the Eastern District of Texas patent infringement action, including at trial and throughout the claims reduction process preceding that trial.

308. Allergan's sole basis for its patent infringement suits against Amneal and Saptalis's were the '162 and '556 patents – the *two patents Allergan dropped from the Eastern District of Texas litigation because they were entirely duplicative of the thirteen patent claims invalidated in that litigation*.

309. Allergan knew that no reasonable litigant would have a realistic expectation of prevailing on the ultimate merits of lawsuits asserting the '162 and '556 patents. But Allergan's purpose in filing and pursuing these two new suits was not to achieve ultimate patent victories; it was to delay any generic from entering the market. By filing these sham suits, Allergan ensured that neither generic would enter the market because, regardless of the suits' merits (or lack thereof), the filing of each suit triggered the automatic, 30-month stay of FDA approval.

310. On January 3, 2019, after relevant subpoenas issued from this Court, Allergan voluntarily dismissed both actions "without prejudice."

M. In the absence of Allergan's scheme to monopolize, generic Restasis would have been available as early as May 2014.

311. Were it not for Allergan's execution of its unlawful scheme, generic Restasis

would have been approved and entered the market as early as May 2014.

312. ANDAs for generic Restasis were submitted to the FDA many years ago; in some cases, over two years before the expiration of the Ding I patent in May of 2014. Given the average amount of time it took the FDA to grant full approval of ANDAs in 2014 (about a year and a half),[173] the lengthy period of time following the submissions of the generic Restasis ANDAs fell well within that time period.

313. Specifically, as to generic Restasis ANDAs, the FDA acknowledged in mid-2015 the filing of several ANDAs. Those acknowledgements constitute a ruling that those ANDAs were substantially complete at the time that they were filed. This indicates that at the time of their submission – in some cases months or years before expiration of the Ding I patent – those applications contained sufficient information from which FDA review and an approval decision could be made.

314. Some of the largest and most sophisticated drug companies had submitted the ANDAs for generic Restasis. The active and inactive ingredients are commonly known, easily available and unprotected by patents. The actual production of cyclosporine ophthalmic emulsion, 0.05% poses little manufacturing or formulation obstacles. To be sure, each ANDA applicant had to meet the challenges posed by the FDA's in vitro testing requirements. But few actual production obstacles stood in the way of readying the drug for distribution.

315. The obstacles Allergan's scheme constructed are of a kind that normally do cause, and are expected to cause, delay of generic entry. Obtaining patents through fraud and then enforcing them burdens ANDA applicants and delays generic entry. In the absence of the

[173] Food & Drug Admin., Performance Report to Congress for the Generic Drug User Fee Amendments 15 (2015).

second wave patents, no patent obstacles would have existed after May 2014. Allergan's decision to list its fraudulent patents in the Orange Book enabled it to file litigation immediately (upon receipt of the Paragraph IV notification) against generic competitor as well as obtain 30-month stays of FDA approval for generics. These listing also create the potential for a 180-day period of generic first-filer exclusivity. Filing petitions to the FDA that were unlikely to change FDA policy further disrupt the ordinary course of the FDA's review and approval of the generic Restasis ANDAs. Despite the FDA's misgivings about the lack of sound, substantive bases for Allergan's citizen petitions, the FDA was nonetheless obligated to respond to each of Allergan's requests. Allergan's rampant litigiousness, including sham transfers of the second wave patents to a Native American tribe to avoid PTO scrutiny, signals to generic manufacturers and the FDA that Allergan will stop at almost nothing to frustrate generic competition.

316. Delay of generic approvals also flows from some FDA statements. For example, in the February 2016 rejection letter, the FDA informed Allergan that it would "not approve or receive any ANDA referencing Restasis based on in vitro assays unless and until FDA responds specifically to the findings of Allergan's testing of nine experimental test emulsions" submitted with the December 2014 Citizen Petition.[174] While that letter itself provided the response needed, the FDA effectively acknowledged that Allergan's petition – although based on faulty science and ultimately having no merit whatsoever – had already delayed its approval of any generic Restasis ANDA.

317. An inference of delay also follows from Allergan's intent and its actions.

[174] More specifically, Allergan submitted data regarding a series of emulsions that were not bioequivalent to Restasis, but Allergan claimed passed the agency's in vitro test. FDA Feb. 2016 Response to Allergan Dec. 2014 Citizen Petition at 24. The FDA pointed out that none of these emulsions, in fact, met the in vitro test, *id.* at 24-26, – a fact that Allergan itself partially admitted. *Id.* at 25-26, 26 n.107. The agency, nevertheless, fully responded to Allergan's claim.

Allergan's acts were intended to have the effect of delaying generic entry. They were not idly undertaken, nor undertaken to improve public health or safety. (Note, for example, Allergan's choice not to bring suit to challenge the FDA's denial of its petitions). It is reasonable to infer Allergan's actions had their intended consequence.

318. The generic industry itself has acknowledged Allergan's delay of generic versions of Restasis. As Mylan's CEO, Heather M. Bresch, has explained, "I think this is a great example of [Mylan] persevering through what I would call [Allergan's] pretty desperate legal maneuvers to try to maintain a monopoly that should have been gone a couple of years ago, and our ability [to] continue to fight not only in the courts, but with the science and have a clear pathway to approvals."[175]

319. Had scientists, regulatory professionals, lawyers, generic manufacturers, and the FDA not been tied up by Allergan's "desperate legal maneuvers," and had they not been forced for years to "continue to fight" Allergan's anticompetitive conduct, they would have remained focused solely on ensuring that safe and effective generic version(s) of Restasis were approved "years ago" at, or as near as possible to, the expiration of the Ding I patent in May 2014. This delay in competition is a direct result of Allergan's anticompetitive scheme and the exact result Allergan intended to achieve.

320. But for Allergan's misconduct, one or several of the ANDA filers would have received FDA approval and would have been able to supply the commercial quantities of generic Restasis necessary to meet market demand upon expiration of the Ding I patent as early as May 2014.

[175] Mylan, *Mylan NV (MYL) Q3 2017 Results – Earning Call Transcript*, Seeking Alpha, at 13 (Nov. 6, 2017), https://seekingalpha.com/article/4121235-mylan-nv-myl-q3-2017-results-earnings-call-transcript?all=true&find=%22and%20on%C2%A0RESTASIS%E2%80%A6.

VI. CLASS ALLEGATIONS

321. Meijer on behalf of itself and all other similarly situated direct purchasers, seeks damages, measured as overcharges, trebled, against Allergan based on allegations of anticompetitive conduct in the market for cyclosporine ophthalmic emulsion, 0.05% (Restasis and its generic equivalents).

322. Meijer brings this action on behalf of itself and, under Fed. R. Civ. P. 23(a) and (b)(3), as representatives of a class of direct purchasers (the "Class" or "Direct Purchaser Class") defined as follows:

> All persons who or entities which purchased Restasis in the United States or its territories and possessions directly from Allergan at any time after May 2014 through and until the anticompetitive effects of Allergan's conduct cease (the "Class Period").
>
> Excluded from the Direct Purchaser Class are Allergan and its officers, directors, management, employees, subsidiaries, or affiliates, and all governmental entities.

323. Members of the Direct Purchaser Class are so numerous that joinder is impracticable. Plaintiffs believe that the Class is composed of scores of entities. Further, the Direct Purchaser Class is readily identifiable from information and records in Allergan's possession.

324. The Plaintiffs' claims are typical of those of the Direct Purchaser Class. All class members were damaged by the same wrongful conduct of Allergan, i.e., they paid artificially inflated prices for cyclosporine ophthalmic emulsion, 0.05% and were deprived of earlier and more robust competition from less-expensive generic Restasis as a result of Allergan's wrongful conduct.

325. The Plaintiffs will fairly and adequately protect and represent the interests of the Direct Purchaser Class. The interests of Plaintiffs are coincident with, and not antagonistic to,

those of the Direct Purchaser Class.

326. The Plaintiffs are represented by counsel with experience in the prosecution of class action antitrust litigation, and with particular expertise in pharmaceutical antitrust class actions.

327. Questions of law and fact common to the members of the Direct Purchaser Class predominate over questions that may affect only individual class members because Allergan has acted on grounds generally applicable to the entire Direct Purchaser Class thereby making overcharge damages with respect to the Class as a whole appropriate. Such generally applicable conduct is inherent in Allergan's wrongful conduct.

328. Questions of law and fact common to the Direct Purchaser Class include:

i. Whether Allergan willfully obtained and/or maintained monopoly power over cyclosporine ophthalmic emulsion, 0.05% products;

ii. Whether Allergan obtained the second wave patents by fraud;

iii. Whether Allergan unlawfully listed the second wave patents in the FDA's Orange Book;

iv. Whether Allergan prosecuted objectively baseless patent litigation with the intent of undermining competition;

v. Whether Allergan filed and pursued objectively baseless citizen petitions with the FDA with the intent of undermining competition;

vi. Whether Allergan's agreement with Mohawk violated Section 1 of the Sherman Act;

vii. Whether Allergan engaged in a scheme to monopolize that violated Section 1 of the Sherman Act;

viii. Whether Allergan unlawfully delayed or prevented generic manufacturers of cyclosporine ophthalmic emulsion, 0.05% from entering the market in the United States;

ix. Whether Allergan's activities substantially affected interstate commerce;

x. Whether, and, if so, to what extent, Allergan's conduct caused antitrust injury (i.e., overcharges) to the Plaintiffs and the Class; and

xi. The quantum of aggregate overcharge damages to the Class.

329. Class action treatment is a superior method for the fair and efficient adjudication of the controversy. Such treatment will permit a large number of similarly situated persons to prosecute their common claims in a single forum simultaneously, efficiently, and without the unnecessary duplication of evidence, effort, or expense that numerous individual actions would engender. The benefits of proceeding through the class mechanism, including providing injured persons or entities a method for obtaining redress on claims that could not practicably be pursued individually, substantially outweighs potential difficulties in management of this class action.

330. The Plaintiffs know of no special difficulty to be encountered in the maintenance of this action that would preclude its maintenance as a class action.

VII. MARKET POWER AND DEFINITION

331. The relevant geographic market is the United States and its territories and possessions.

332. At all relevant times, Allergan's share of the relevant cyclosporine ophthalmic emulsion, 0.05% market was and remains 100%.

333. At all relevant times, Allergan had monopoly power in the market for cyclosporine ophthalmic emulsion, 0.05% products. It had the power to maintain the price of Restasis at supra-competitive levels without losing substantial sales to other products prescribed

and/or used for the same purposes as Restasis, with the exception of generic cyclosporine ophthalmic emulsion, 0.05% products. This market power may be shown directly, and therefore no relevant market needs to be defined.

334. Allergan has admitted that it holds 100% of the relevant market. In October of 2013, Allergan's vice president of marketing swore, under oath that "[a]s there is no other FDA-approved therapeutic treatment for dry eye available on the US market, Restasis own 100% of the market share."[176] Allergan's patent counsel repeated that statement in a PTO filing.

335. Allergan has enjoyed the monopoly power conferred by the Ding I patent from 1995 to May of 2014. It procured the second wave patents to further extend that monopoly.

336. Since 2003, when it launched Restasis, Allergan has reaped significant commercial benefits. When it received FDA approval for Restasis in December 2002, Allergan advertised Restasis as "the first and only therapy for patients with keratoconjunctivitis sicca (chronic dry eye disease-CDED) whose tear production is presumed to be suppressed due to ocular inflammation."[177] In its numerous filings with the FDA, Allergan similarly characterized Restasis' uniqueness: "Restasis is a pathbreaking product that was developed to treat the widespread and sometimes debilitating problem of dry eye disease. Before Restasis, dry eye disease was a largely unmet medical need. After years of FDA-required clinical trials, Allergan was able to produce a precisely formulated drug that has significant efficacy in treating dry eye

[176] Declaration of Aziz Mottiwala before the U.S. Patent and Trademark Office (Oct. 8, 2013).

[177] Press Release, Allergan, Allergan's Restasis Approved by the FDA; The First and Only Therapeutic Treatment To Increase Tear Production in Patients with Chronic Dry Eye Due to Ocular Inflammation (Dec. 24, 2002), http://www.evaluategroup.com/Universal/View.aspx?type=Story&id=35422.

disease."[178]

337. Manufacturers attempt to differentiate brand name drugs like Restasis based on features and benefits (including safety and efficacy), and not based on price. Doctors and patients are generally price-insensitive when prescribing and taking prescription drugs like Restasis. This is due in part to the presence of insurance that bears much of the cost of prescriptions and other institutional features of the pharmaceutical marketplace. Different patients may respond differently to different drugs and even drugs within its same therapeutic class do not constrain the price of Restasis.

338. Other products are not practical substitutes for cyclosporine ophthalmic emulsion, 0.05%. Artificial tears offer only transient symptomatic relief and do nothing to address the underlying causes of dry eye. Corticosteroids can address the inflammation associated with dry eye, but have unwanted side effects, as do devices such as punctal plugs, which block the tear ducts and help the eye retain naturally produced tears for longer. Patients treated with cyclosporine ophthalmic emulsion, 0.05% would not switch to these products in response to a small but significant non-transitory increase in the price of cyclosporine ophthalmic emulsion, 0.05% in sufficient numbers to make such a price increase by a hypothetical monopolist unprofitable. Shire US, Inc.'s introduction last year of its rival dry-eye disease product, Xiidra, has not resulted in lower Restasis prices, thus confirming Allergan's continued market power over the relevant cyclosporine ophthalmic emulsion, 0.05% market.

339. Allergan's ability to double the price of Restasis over the past decade without loss of significant sales further demonstrates lack of substitutability between Restasis and other drug

[178] February 2014 Citizen Petition at 13.

products.[179] Restasis does not exhibit significant, positive cross-elasticity of demand with respect to price with any other dry-eye medication. Other various dry-eye treatments may exist, but none exhibit cross price elasticity with Restasis and therefore do not constrain the price of Restasis. The existence of these non-cyclosporine products that may be used to treat similar indications did not constrain Allergan's ability to raise or maintain Restasis prices without losing substantial sales, and therefore those other drug products are not in the same relevant antitrust market as Restasis. Therapeutic alternatives, to the extent existent, are not the same as economic alternatives.

340. Functional similarities between Restasis and other dry-eye medications, other than generic Restasis equivalents, are insufficient to permit inclusion of those other molecules in the relevant market with Restasis. To be an economic substitute for antitrust purposes, a functionally similar product must also exert sufficient pressure on the prices and sales of another product, so that the price of that product cannot be maintained above levels that would otherwise be maintained in a competitive market. No other dry-eye medication (except for generic versions of Restasis) will take away sufficient sales of Restasis to prevent Allergan from raising or maintaining the price of Restasis above levels that would otherwise prevail in a competitive market.

341. Restasis is also not reasonably interchangeable with any products other than generic versions of Restasis because Restasis has significantly differentiating attributes making it a unique drug product. The FDA does not consider Restasis interchangeable with any other

[179] *See* David Crow, *Allergan Deal with Mohawk Tribe Casts Patent Shadow*, Fin. Times (Sept. 27, 2017), https://www.ft.com/content/5ec7305a-9f17-11e7-9a86-4d5a475ba4c5 ("The average wholesale price of a 30-dose pack of Restasis has more than doubled from $117 in 2008 to almost $280 today").

medication. Nor does Allergan. For example, Restasis is a topical ophthalmic formulation, and as Allergan has explained, "[u]nlike other drug delivery routes, a topical ophthalmic formulation must deliver drug to the ocular tissues in the relatively short timeframe of only a few minutes."[180]

342. Allergan needed to control only Restasis and its generic equivalents, and no other products, to maintain the price of Restasis at a supra-competitive level while preserving all or virtually all of its sales. Only the market entry of a competing, generic version of Restasis would render Allergan unable to maintain its monopoly prices of Restasis without losing substantial sales.

343. Allergan also sold Restasis at prices well in excess of marginal costs, and substantially in excess of the competitive price, and enjoyed high profit margins.

344. Allergan has exercised its power to exclude and restrict competition to Restasis and its generic equivalents.

345. Allergan, at all relevant times, enjoyed high barriers to entry with respect to competition in the relevant product market of cyclosporine ophthalmic emulsion, 0.05% due, in large part, to legally and illegally created patent protections, legally and illegally created regulatory bars to FDA approval of generic competitors, and high costs of entry and expansion.

346. To the extent Plaintiffs are legally required to prove monopoly power through circumstantial evidence by first defining a relevant product market, Plaintiffs allege that the relevant market is all cyclosporine ophthalmic emulsion, 0.05% products (i.e., Restasis and its generic equivalents). During the period relevant to this case, Allergan has been able to profitably maintain the price of cyclosporine ophthalmic emulsion, 0.05% products well above competitive

[180] February 2014 Citizen Petition at 18.

levels.

VIII. MARKET EFFECTS AND CLASS DAMAGES

347. But for the anticompetitive conduct alleged above, multiple generic manufacturers would have entered the market with their generic cyclosporine ophthalmic emulsion, 0.05% products starting as early as May 2014, when the exclusivity associated with Ding I expired.

348. Instead, Allergan willfully and unlawfully maintained its monopoly power in the market for cyclosporine ophthalmic emulsion, 0.05% through a scheme to exclude competition. The scheme forestalled generic competition and carried out its anticompetitive effect of maintaining supra-competitive prices for Restasis. Allergan implemented its scheme by fraudulently obtaining the second wave patents, listing these invalid patents in the Orange Book, enforcing those patents against the generic manufacturers, submitting baseless citizen petitions to the FDA, otherwise abusing the Hatch-Waxman framework, and entering into an anti-competitive agreement with Mohawk to insulate the second wave patents from invalidation in PTO *inter partes* proceedings. These acts, individually and in combination, were anticompetitive.

349. If Allergan had not defrauded the PTO, (1) the second wave patents would never have been issued, and (2) Allergan could never have used those second wave patents as vehicles to bring suits.

350. Allergan's anticompetitive conduct had the purpose and effect of restraining competition unreasonably and injuring competition by protecting Restasis from generic competition. Allergan's actions allowed it to maintain a monopoly and exclude competition in the market for cyclosporine ophthalmic emulsion, 0.05%, i.e., Restasis and its generic equivalents, effectively preserving the market solely for the benefit of Allergan's monopoly profits.

351. Allergan's exclusionary conduct has delayed, prevented, and impeded the efficient sale of and competition from generic cyclosporine ophthalmic emulsion, 0.05% in the United States and unlawfully enabled Allergan to sell Restasis without generic competition (at artificially inflated prices).

352. Allergan's anticompetitive conduct, which delayed the introduction into the U.S. marketplace of any generic version of Restasis, caused Plaintiffs and members of the Class to pay more than they would have paid for cyclosporine ophthalmic emulsion, 0.05%.

IX. ANTITRUST IMPACT

353. During the relevant period, Plaintiffs and members of the Class purchased substantial amounts of Restasis directly from Allergan. As a result of Allergan's unlawful anticompetitive conduct, Plaintiffs and members of the Class were compelled to pay, and did pay, artificially inflated prices for cyclosporine ophthalmic emulsion, 0.05%. Those prices were substantially greater than the prices that Plaintiffs and members of the Class would have paid absent the illegal conduct alleged herein, because: (1) the price of brand-name Restasis was artificially inflated by Allergan's illegal conduct, and (2) class members were deprived of the opportunity to purchase lower-priced, generic versions of Restasis sooner.

354. As a consequence, Plaintiffs and members of the Class have sustained substantial losses and damage to their business and property in the form of overcharges. The full amount and forms and components of such damages will be calculated after discovery and upon proof at trial.

X. CLAIMS FOR RELIEF

COUNT I
Violation of Section 2 of the Sherman Act, 15 U.S.C. § 2:
Monopolization Through *Walker Process* Fraud

355. Plaintiffs repeat and incorporate by reference all preceding paragraphs and allegations.

356. As described above, from 1995 until the present (and with continuing effects hereafter), Allergan possessed and continues to unlawfully possess monopoly power in the market for cyclosporine ophthalmic emulsion, 0.05%. During the relevant time period, no other manufacturer sold a competing version of cyclosporine ophthalmic emulsion, 0.05% in the United States.

357. Allergan has willfully and unlawfully maintained its monopoly power in the cyclosporine ophthalmic emulsion, 0.05% market from May 2014 through at least the present day by acquiring through fraud, and then enforcing, the second wave patents to keep generic equivalents off the market. Allergan's monopoly during this period was not the result of its provision of a superior product, business acumen, or historical accident.

358. Allergan knowingly and intentionally asserted the invalid second wave patents in order to maintain its monopoly power. Allergan's assertion of these patents was intended to and had the effect of blocking and delaying entry of generic versions of Restasis.

359. Allergan, by and through its patent attorneys and scientists who submitted declarations in support of patentability (including Laura L. Wine, Dr. Rhett M. Schiffman, and Dr. Mayasa Attar), made misrepresentations of fact to the PTO. Including, but not limited to,

- Allergan's patent counsel stated that Dr. Schiffman's declaration showed "surprisingly, the claimed formulation demonstrated an 8-fold increase in relative efficacy for the Schirmer Teat Test score in the first study of Allergan's Phase 3 trials compares to the relative efficacy for the . . . formulation discussed in Example 1E of Ding, tested in Phase 2 trials . . . This was clearly a very surprising and unexpected result."

- Allergan's patent counsel stated that Dr. Schiffman's declaration showed "the claimed formulations also demonstrated a 4-fold improvement in the relative

efficacy for the Schirmer Tear Test score for the second study of Phase 3 and a 4-fold increase in relative efficacy for decrease in corneal staining scores in both of the Phase 3 studies compared to the . . . formulation tested in Phase 2 and disclosed in Ding. This was clearly a very surprising and unexpected result."

- Allergan and Dr. Schiffman did not disclose to the PTO that figures 1-4 in Dr. Schiffman's declaration, which copied figures from the Sall paper, omitted all error bars and p-values that were included in Sall's figures. In truth, as the *Allergan* court later found, none of the pair-wise comparisons between the two cyclosporine formulations for corneal staining and Schirmer scores in the Phase 2 study or the pooled Phase 3 studies demonstrated statistical significance at any time point and many of the p-values for the pair-wise comparisons were very high. The actual statistical analyses showed that any observed difference in outcomes between the cyclosporine formulations was likely the result of random chance.

- Allergan and Dr. Schiffman did not disclose to the PTO that he was comparing different Schirmer tear test scores and at different time points – Schirmer tests *without* anesthesia at *12 weeks* in Phase 2 to Schirmer tests *with* anesthesia at *6 months* in Phase 3 – to purportedly show a difference in efficacy. "It was [] only by comparing the results of two different types of tests that Dr. Schiffman was able to produce a significantly distorted picture suggesting that the 0.05% cyclosporin/1.25% castor oil formulation in Phase 3 was much more effective than the 0.05% cyclosporin/0.625% castor oil formulation in Phase 2."[181] This comparison was both scientifically and clinically unsound and misled the PTO as to the importance of Dr. Schiffman's results.

- Dr. Schiffman did not disclose to the PTO that the method he used to calculate the differences in efficacy "exaggerated the difference between the 0.05% and 0.1% formulations."[182] More specifically,

    - Dr. Schiffman did not disclose to the PTO that the outcomes he used in his calculations were medians, whereas all other outcomes (in the Sall figures) were means. Dr. Schiffman used a ratio-of-ratios-of-medians methodology, which grossly misrepresented the data and overstated the differences between the results;

    - Dr. Schiffman hid from the PTO and ignored the fact that the Phase 2 study was designed as a pilot study with only fifteen patients per formulation group, whereas the pooled Phase 3 trial had sixteen times that

[181] *Allergan*, 2017 WL 4803941, at *37.

[182] *Id.* at *38.

number per formulation group; and

- Dr. Schiffman only included outcomes from data he found favorable (that is, cherry-picked medians) to make comparisons between the two formulations. He omitted the vast majority of results that did not support his thesis.

- Dr. Schiffman did not tell the PTO that the figures he relied on in his declaration were lifted from the Sall paper, published a decade earlier (and three years before the priority date for the second wave patents). Thus, even if the results presented were surprising (and they were not), they were publicly known before the date of invention and therefore cannot be the basis for a claim that they were "unexpected" as of second wave patents' priority date.

360. These misrepresentations were material. The examiner had repeatedly rejected Allergan's previous applications – applications that were almost identical – as obvious before Allergan submitted this misleading declaration. The examiner had also previously rebuffed Allergan's purported secondary considerations of non-obviousness (including commercial success and unmet need). The Board's decision as well as the United States District Court for the Eastern District of Texas's decision support the materiality of these misrepresentations and omissions.

361. Allergan made these statements with intent to deceive the PTO. The misleading statements were made intentionally, not accidentally. Allergan was motivated to obtain a longer period of patent protection, given the large sales of Restasis and the importance of the product to the company. The misleading statements were only made after the examiner rejected the application (not with the initial filing) and were made to overcome a rejection and support patentability. There is no innocent explanation for presenting the information as Allergan presented it in its misleading declaration and accompanying submissions; the only reasonable inference is that Allergan intended to deceive the PTO.

362. The PTO reasonably relied on Allergan's false and misleading statements in issuing the second wave patents. The examiner stated that the Schiffman and Attar declarations

were deemed sufficient to overcome her earlier rejection based on Ding I because the "[e]xaminer is persuaded that, unexpectedly, the claimed formulation . . . demonstrated an 8-fold increase in relative efficacy for the Schirmer Tear Test score in the first study of Phase 3 trials compared to the relative efficacy for the 0.05% by weight cyclosporin A/0.0625% by weight castor oil formulation disclosed in . . . Ding [I]."[183] The examiner also explained that Allergan's declarations "illustrate that the claimed formulations . . . also demonstrated a 4-fold improvement in the relative efficacy for the Schirmer Tear Test score for the second study of Phase 3 and a 4-fold increase in relative efficacy for decrease in corneal staining score in both of the Phase 3 studies compared to the . . . formulation tested in Phase 2 and disclosed in Ding [I]."[184]

363. But for Allergan's misrepresentations and omissions, the second wave patents would not have issued. Had they not issued, there would have been no patent-based impediment to generic versions of Restasis entering the market from May 2014 onwards.

364. Allergan listed the second wave patents in the Orange Book and later asserted them against all would-be generic competitors.

365. But for Allergan's assertion of its fraudulently obtained patents, generic versions of Restasis would have been available as early as May 2014, and, in any case, within the Class Period.

366. There is no valid procompetitive business justification for Allergan's anticompetitive conduct, and to the extent Allergan offers one, it is pre-textual and not cognizable. Any procompetitive benefits of Allergan's conduct do not outweigh its anticompetitive harms.

COUNT II

[183] *Id.* at *11 (quoting the examiner).

[184] *Id.* (quoting the examiner).

Violation of Section 2 of the Sherman Act, 15 U.S.C. § 2:
Monopolization Through an Overarching Anticompetitive Scheme

367. Plaintiffs repeat and incorporate by reference all preceding paragraphs and allegations.

368. As described above, from 1995 until the present (and with continuing effects hereafter), Allergan possessed and continues to unlawfully possess monopoly power in the market for cyclosporine ophthalmic emulsion, 0.05%. During the relevant time period, no other manufacturer sold a competing version of any cyclosporine ophthalmic emulsion. 0.05% product in the United States.

369. Allergan has willfully and unlawfully maintained its monopoly power in the market for cyclosporine ophthalmic emulsion, 0.05% from May 2014 through at least the present day by engaging in an anticompetitive scheme to keep generic equivalents from the market – not as a result of providing a superior product, business acumen, or historical accident.

370. Allergan knowingly and intentionally engaged in an anticompetitive scheme to maintain its monopoly power, the components of which either standing alone or in combination (in whole or part) were designed to and in fact have blocked and delayed entry of generic versions of Restasis. This scheme included:

- Prosecuting serial, baseless patent applications and ultimately obtaining the second wave patents by fraud through misleading the PTO and failing to comply with the duty of disclosure, candor, and good faith;
- Unlawfully listing the second wave patents in the Orange Book;
- Wrongfully enforcing the second wave patents in multiple lawsuits;
- Submitting serial baseless citizen petitions; and
- Abusing the Patent Trial and Appeal Board's *inter partes* review process through an anticompetitive transfer of the second wave patents to the Saint Regis Mohawk Tribe.

371. By means of this scheme, Allergan intentionally and wrongfully maintained monopoly power with respect to Restasis in violation of Section 2 of the Sherman Act. As a result of this unlawful maintenance of monopoly power, Plaintiffs and members of the Class paid artificially inflated prices for cyclosporine ophthalmic emulsion, 0.05%.

372. Plaintiffs and members of the Class have been injured in their business or property by Allergan's antitrust violations. Their injury consists of having paid higher prices for cyclosporine ophthalmic emulsion, 0.05% than they would have paid in the absence of Allergan's violations. Such injury, called "overcharges," is of the type antitrust laws were designed to prevent, flows from that which makes Allergan's conduct unlawful, and Plaintiffs and the Class are the proper entities to bring a case concerning this conduct.

373. Allergan knowingly and intentionally committed *Walker Process* fraud to induce the PTO to grant the second wave patents. Allergan – after the PTO's repeated denials of prior substantially similar serial applications over more than a 10-year period – submitted false sworn declarations in 2013, that Allergan characterized, by commission and omission, as presenting new data that showed surprising results not anticipated by prior art (i.e., Ding I), when in fact the data presented was neither new or surprising. Had Allergan made clear to the PTO examiner that the 2013 declarations statements and data were lifted from prior art known to Allergan for over thirteen years (and which had been published three years before the September 2003 priority date), the PTO examiner would have rejected all of the 2013 applications for the same reasons it had repeatedly denied every prior application: that the claims presented were obvious in light of prior art. Allergan's misstatements were material, fraudulent, and made knowingly and with the intent to deceive. They induced the PTO to issue the second wave patents.

374. Allergan knew when it listed the second wave patents in the Orange Book that

those patents were fraudulently procured and/or were otherwise invalid as obvious in light of prior art, namely Ding I and the related patents and the Stevenson and Sall papers. Therefore, Allergan knew the second wave patents should not have been listed in the Orange Book. Allergan knew that listing the second wave patents in the Orange Book would force ANDA applicants to file Paragraph IV certifications that would then provide Allergan the opportunity to file baseless patent infringement suits against those ANDA applicants. Allergan also knew these lawsuits could trigger automatic stays of FDA final approval of new, Paragraph IV-certified ANDA applications to manufacture generic Restasis for a period of up to 30 months. And by obtaining and/or listing the first second wave patent in the Orange Book, Allergan created regulatory challenges that could slow or forestall the FDA ANDA approval process.

375. Allergan knowingly and intentionally engaged in multiple sham litigations against manufacturers of generic equivalents of Restasis that no reasonable pharmaceutical company in Allergan's position would realistically expect to win. Allergan intentionally and deceptively alleged the generic manufacturers' products infringed its second wave patents, knowing when those suits were filed that such patents were obtained though fraud on the PTO and were otherwise invalid as obvious in light of the prior art. Allergan also knew, at the time those multiple sham suits were filed, that it had no realistic likelihood of success, i.e., that there was no realistic likelihood that a court would enforce the fraudulently-obtained and otherwise invalid second wave patents against a generic company. Allergan knew, therefore, that no reasonable pharmaceutical manufacturer would have believed it had a reasonable chance of succeeding on the merits of those infringement lawsuits. Allergan filed those sham lawsuits for the purposes of using a governmental process as an anticompetitive weapon to keep generics off the market and wrongfully maintain its monopoly power over Restasis, regardless of any actual merit to its

infringement claims.

376. Allergan knowingly and intentionally submitted multiple citizen and other petitions to the FDA when no reasonable pharmaceutical manufacturer in Allergan's position would expect the FDA to grant the requested relief. The purpose and intent of these petitions was to delay the FDA's approval of any of the pending generic ANDA applications, regardless of any objective merit of any part of the petitions.

377. Allergan knowingly and intentionally transferred the second wave patents to Mohawk – a sovereign tribe that does not manufacture or distribute pharmaceutical products of any kind – in an attempt to evade invalidation of those patents and cessation of its Restasis monopoly. This conduct illustrates the extraordinary measures Allergan was willing to take to delay competition.

378. Allergan's anticompetitive conduct is not entitled to any qualified *Noerr-Pennington* immunity, nor is it protected by the state action doctrine.

379. There is no valid procompetitive business justification for Allergan's anticompetitive conduct, and to the extent Allergan offers one, it is pre-textual and not cognizable. Any procompetitive benefits of Allergan's conduct do not outweigh its anticompetitive harms.

COUNT III
Violation of Section 1 of the Sherman Act, 15 U.S.C. § 1:
Contract in Restraint of Trade

380. Plaintiffs repeat and incorporate by reference all preceding paragraphs and allegations.

381. Allergan entered into a contract with Mohawk in unreasonable restraint of trade in violation of Section 1 of the Sherman Act, 15 U.S.C. § 1.

382. Allergan's contract in restraint of trade and its other anticompetitive acts were intentionally directed at the United States Restasis market and had a substantial and foreseeable effect on interstate commerce by interfering with potential generic competition for Restasis and raising and maintaining Restasis prices at supra-competitive levels throughout the United States.

383. As a result of the contract in restraint of trade, Allergan and Mohawk have effectively excluded competition from the Restasis market, allowing Allergan to unlawfully maintain its monopoly in the Restasis market, and both Allergan and Mohawk have profited from their illegal contract by maintaining prices at artificially high levels.

384. There is no legitimate business justification for the anti-competitive actions of Allergan and Mohawk and the conduct through which Allergan maintained its monopoly in the market, including the contract between Allergan and Mohawk. The anticompetitive effects of Allergan's and Mohawk's contract far outweigh any conceivable pro-competitive benefit or justification.

385. As a direct and proximate result of Allergan's and Mohawk's unlawful actions, Plaintiffs and members of the Class were injured in their business or property.

386. As a direct and proximate result of Allergan's and Mohawk's unlawful actions, Plaintiffs and the other members of the Class have been forced to pay artificially high, supra-competitive prices for Restasis and were harmed by such prices.

387. Plaintiffs and members of the Class are entitled to treble damages to remedy the injuries they have suffered from Allergan's violations of Sherman Act § 1, 15 U.S.C. § 1.

COUNT IV
Violation of Section 2 of the Sherman Act, 15 U.S.C. § 2:
Conspiracy to Monopolize

388. Plaintiffs repeat and incorporate by reference all preceding paragraphs and

allegations.

389. Allergan and Mohawk have conspired to allow Allergan to willfully maintain and unlawfully exercise monopoly power in the Restasis market through their anti-competitive contract with the specific intent to monopolize the Restasis market, and preventing competition in the market.

390. As a result of the conspiracy, Allergan and Mohawk have effectively excluded competition from the Restasis market, unlawfully maintained Allergan's monopoly in the Restasis market, and profited from their anti-competitive conduct by maintaining prices at artificially high levels.

391. As a result of the contract in restraint of trade, Allergan and Mohawk have effectively excluded competition from the Restasis market, allowing Allergan to unlawfully maintain its monopoly in the Restasis market, including the contract between Allergan and Mohawk. The anti-competitive effects of Allergan's and Mohawk's contract far outweigh any conceivable pro-competitive benefit or justification.

392. There is no legitimate business justification for the anti-competitive actions of Allergan and Mohawk and the conduct through which Allergan maintained its monopoly in the market. The anti-competitive effects of Allergan's and Mohawk's agreement far outweigh any conceivable pro-competitive benefit or justification.

393. As a direct and proximate result of Allergan's and Mohawk's unlawful actions, Plaintiffs and members of the Class have been and continue to be injured in their business or property.

394. As a direct and proximate result of Allergan's and Mohawk's unlawful actions, the Plaintiffs and the other members of the Class have been forced to pay artificially high, supra-

competitive prices for Restasis and were harmed thereby.

395. Plaintiffs and members of the Class are entitled to treble damages to remedy the injuries they have suffered from Allergan's violations of Sherman Act § 2, 15 U.S.C. § 2.

XI. DEMAND FOR RELIEF

WHEREFORE, Plaintiffs, on behalf of itself and the proposed class, respectfully demands that the Court:

i. Determine that this action may be maintained as a class action pursuant to Fed. R. Civ. P. Rule 23(a) and (b)(3), direct that reasonable notice of this action, as provided by Rule 23(c)(2), be given to the Class, and declare Meijer as named representatives of the Class;

ii. Conduct expedited discovery proceedings leading to a prompt trial on the merits before a jury on all claims and defenses;

iii. Enter judgment against Allergan and in favor of the Plaintiffs and the Class;

iv. Award damages (i.e., three times overcharges) to the Class in an amount to be determined at trial, plus interest in accordance with law;

v. Award Plaintiffs and the Class their costs of suit, including reasonable attorneys' fees as provided by law; and

vi. Award such further and additional relief as is necessary to correct for the anticompetitive market effects Allergan's unlawful conduct caused and as the Court may deem just and proper under the circumstances.

XII. JURY DEMAND

Pursuant to Rule 38 of the Federal Rules of Civil Procedure, the Plaintiffs, on behalf of themselves and the proposed Class, demands a trial by jury on all issues so triable.

Dated: May 1, 2019

Respectfully submitted,

/s/ David S. Nalven

David S. Nalven (E.D.N.Y. Barcode: DS2374)
Thomas M. Sobol
Kristen A. Johnson
Jessica R. MacAuley
Hannah W. Brennan
HAGENS BERMAN SOBOL SHAPIRO LLP
55 Cambridge Parkway
Suite 301
Cambridge, MA 02142
Tel: (617) 482-3700
Fax: (617) 482-3003
davidn@hbbslaw.com
tom@hbsslaw.com
kristenj@hbsslaw.com
jessicam@hbsslaw.com
hannahb@hbsslaw.com

/s/ Paul E. Slater

Paul E. Slater
Joseph M. Vanek
David P. Germaine
John P. Bjork
SPERLING & SLATER, P.C.
55 W. Monroe Street, Suite 3200
Chicago, Illinois 60603
Tel: (312) 641-3200
Fax: (312) 641-6492
pes@sperling-law.com
jvanek@sperling-law.com
dgermaine@sperling-law.com
jbjork@sperling-law.com

Counsel for Meijer, Inc. & Meijer Distribution, Inc.